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SOME SOCIOLOGIC AND PSYCHOLOGIC OBSERVATIONS ON ABORTION*

A STUDY OF 537 CASES

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THAT induced abortion is primarily a sociologic and psychologic problem is self-evident. If conditions did not exist which make offspring undesirable, to the particular woman at the particular time, there would be no induced abortion. If every married woman felt her family budget sufficient to provide satisfactorily for unlimited children, if there were no social stigma associated with illegitimacy, the incidence of induced abortion would, no doubt, be reduced to a fraction of its present magnitude. The relative nature of economic and social pressure must be stressed. An income which would seem ample for four children to a woman accustomed to one standard of living would seem to another hopelessly inadequate for one. Illegitimacy is accepted in certain social groups with no more than a passing sneer, in others it means ruin to the mother and lifelong handicap to the child. Other, more subtle, factors play a part in the problem. These, too, vary from group to group and from woman to woman within the group. Aleck Bourne has recently presented an analysis of these factors in an address to the Edinburgh Obstetrical Society which for clarity and good sense excels any similar discussion known to the author.

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Social, economic, and psychic factors are less obviously related to spontaneous abortion. Nevertheless their indirect influence must be acknowledged. Dramatic cases in which violent emotions, fear, grief, anger, are followed by the immediate onset of labor pains and vaginal bleeding, are well authenticated. These are the exception. That the mixed psychologic and sociologic factors of poverty, toil, anxiety, defective diet, and neglected health contribute to spontaneous abortion, while more difficult to prove, appear obvious. That these factors are often ineffective in interrupting pregnancy is, of course, shown by the number of children carried to term by women who are burdened by them all.

It is unnecessary to point out the major importance of the abortion problem. The estimates of its magnitude as presented conservatively by Taussig are too familiar to be repeated here. The reason that these estimates are so familiar is that Taussig's is actually the only book in the English language which even attempts a comprehensive analysis of the subject. Considering its great social significance, it is truly incredible that so little has been written about abortion. The extent of our ignorance is boundless. That is the only excuse for presenting the crude and incomplete data offered here.

In a fairly diligent search for series comparable to the present one, only 14 papers which analyze groups of cases admitted to hospital under the diagnosis of "abortion" and which offer any descriptive data on the sample of population involved have been found in the English and American medical literature of the past ten years. Even in these, the data are meager in the extreme, color, marital status, and religion being usually all that is reported.

The question of whether or not the abortion was induced assumes paramount importance in the minds of most investigators. The majority, however, note the impossibility of certainty in obtaining an answer to this question.

There is no reasonable doubt that many patients deliberately and persistently lie in denying induction. Their motives are fear of punishment or moral censure and/or loyalty to the abortionist whom they consider their helper. There is also little doubt that others who admit induction freely are the dupes of coincidence and have actually undergone a spontaneous abortion soon after taking a hot bath or a cup of ginger tea. Still others, in both groups and also in the group who convincingly claim that they have had a "miscarriage," prove actually to be suffering from various pelvic conditions unassociated in any way with pregnancy. The latter group is particularly interesting because of its vitiation of any statistical study based on the statement of the patient about her past history. In our series of 537 cases there were 67 (12.4 per cent) whose final diagnosis was "not pregnant." Twenty-two of these patients will go around for the rest of their lives glibly telling all history takers that they had an "abortion," while 45 will as freely state that they had a "miscarriage."

The difficulties in arriving at a correct appraisal of circumstances surrounding the abortion do not stop when the momentous question "in-

duced" or "spontaneous" is answered. Intentional deception, unintentional misinterpretation, and candid truth-telling mingle in varying proportions in the mass response to each question. Many of the answers undoubtedly represent the patient's idea of what *ought* to be the case and are a half-conscious attempt to deceive not only the investigator, but herself as well. The overwhelming majority of married women who said they loved their husbands is an example. The few who expressed dislike went against convention and did so with an effort. Conversely it is conventional for a single girl to abhor her seducer, hence those who declare that they "still love him" do so with bravado.

The same applies to the statement of childhood experience. Those who loyally claim that they had happy homes and that their fathers provided amply for all their needs are probably far in excess of the actual number who were brought up under these idyllic circumstances. Recognizing the practical impossibility of disentangling the true from the false or equivocal and with the profound humility of an investigator who does not set up to be in any sense a sociologist or a psychologist, the author presents the following data in the hope that others who are better qualified may be inspired to dig more deeply into the mine which is here barely opened.

Although the group who admitted drug or thermal induction conform clinically much more closely to those whom we believe to have had truly spontaneous abortions, and although a subgroup of those who denied induction, that subgroup which the examiner considered untruthful, conforms in most respects to the mechanically induced group, we have thought best in this particular study to make our classification purely on the basis of the patient's statement. We are concerned here not with treatment nor prognosis, but with motivation and behavior. The woman who soaks her feet in mustard water and takes pills has the same purpose in mind as the one who visits the abortionist. Hence our cases are divided into "induced" and "spontaneous" according to the patient's admission or denial that she voluntarily did anything with the intention of interrupting the normal course of her pregnancy.

Beginning May 1, 1938 and continuing almost daily until July 15, 1939, the author interviewed all but 50 of 537 consecutive patients who were admitted to the Gynecological Ward of Bellevue Hospital for symptoms associated with an interruption of pregnancy before the twenty-eighth week. The 50 patients excepted were interviewed by Dr. Katherine Miller. Admission diagnosis included threatened, inevitable, incomplete, complete, and missed abortion and also 30 cases referred from the medical service for therapeutic abortion. An effort was made to see all patients within twenty-four hours of admission and before active treatment, as it was thought that they would talk more freely if they felt that the interview had some immediate bearing on the care they would receive. The interview was as nearly private as ward conditions would permit, and, when necessary to gain cooperation, the patients were assured that the information they gave was strictly confidential, would not be filed under their names, and would not be included in their hospital records. They were encouraged

to tell their stories freely, but were interrupted for answers to specific questions where those did not appear spontaneously. An effort was made to refrain from leading questions. Each interview occupied from one-half to one hour and many patients were visited repeatedly on successive days. Several who denied induction at the first questioning later admitted it. Two, who were most persistent in denial, in terminal delirium described their experience with the abortionist. At the end of the interview a note of the examiner's estimate of the patient's reliability was made. True, false, or doubtful applied principally to the statement of induction, since many patients appeared perfectly candid in their answers to all other questions, deceptive on that point alone. As a whole the group showed surprisingly little reluctance to discuss the intimate questions which were put to them. A few seemed disinclined to discuss their sex life. These were not pressed to do so.

It seems hardly necessary to point out the extreme selection evidenced by the very admission of these patients to Bellevue. This fact alone places the overwhelming majority in those much discussed fractions of our total population, the "one-third of a nation" whose housing conditions are atrocious and the "submerged tenth" whose finances never were and possibly never will be consistent with even a modest standard of comfortable living. The unwisdom of applying any observation here recorded to any other population group is self-evident. Ideas of economic sufficiency are relative, however, human nature does not vary greatly and the same motives, reactions, and attitudes may be found, though doubtless in varying proportions in other groups of "higher society."

MATERIAL

Our group consisted of 156 patients (29 per cent) who admitted induction, 346 (64.5 per cent) who denied it, and 30 (5.5 per cent) who were referred for therapeutic abortion. Five, diagnosed "abortion" on admission, proved to have ectopic pregnancies and were included in the therapeutic group, raising it to 35. Seventy-two per cent were married women, 12 per cent single, and 16 per cent previously married (widowed, separated, or divorced). The low proportion of married women as compared to other series in this country (80 to 92.3 per cent) may be due to the high proportion of negroes in our sample (34 per cent). Of these, only 59 per cent were married and still living with their husbands. It may also be due to our classification, as in several of the other studies only two categories are considered, ever married and single. The latter classification would give us 88 per cent married women, 92 per cent white married, and 68 per cent negro married. Among the married, color plays no significant part in the type of abortion. Twenty-two per cent of the white married women admitted induction, 24 per cent of the negro. The difference in behavior between the white and negro single groups is significant. Sixty-four of the single white women admitted induction, while but 40 per cent of the unmarried negroes did so. Still more striking is the difference between the two previously married groups; the negroes behaving essentially like those still married (28 per cent), while the whites showed nearly twice the frequency of induction (52 per cent) (Table I).

Our patients varied in age from 13 to 49 years. Neither of the extreme cases was found to have been pregnant. Although the little girl admitted coitus and although her mother had plied her with oxytocics, the pathologic report established her diagnosis as cystic and glandular endometrial hyperplasia. The older woman, though equally chagrined by the prospect of an addition to her family, proved to be suffering from fibromyoma uteri. The youngest actual abortion case was 15,

TABLE I. PATIENT'S STATEMENT OF TYPE OF ABORTION, EXAMINER'S ESTIMATE OF VERACITY, COLOR AND MARITAL STATUS

	CASES	%	INDUCED (MECH.)	%	INDUCED (DRUG)	%	SPONT. (FALSE)	%	SPONT. (DOUBT.)	%	SPONT. (TRUE)	%	THERA.	%
White	353	100	42	12	62	18	21	6	88	25	112	32	28	7
Married	279	79	23	8	39	14	13	5	75	27	108	39	21	7
Previously married	46	13	7	15	17	37	5	11	11	24	2	4	4	9
Single	28	8	12	43	6	21	3	11	2	7	2	7	3	11
Negro	184	100	10	5	42	23	11	6	68	37	46	25	7	4
Married	108	59	5	5	21	19	4	4	36	33	38	35	4	4
Previously married	36	19	-	-	10	28	3	8	15	42	5	14	3	8
Single	40	22	5	12	11	28	4	10	17	43	3	7	-	-
Totals	537	100	52	10	104	19	32	6	156	29	158	29	35	7

the oldest 47. As in all comparable series, the great majority (73 per cent) of patients were between 20 and 35. More than half (57 per cent) were between 20 and 30. The average age for all patients was 27.8 years. For those admitting induction it was nearly a year younger, 26.9. No appreciable difference in age distribution could be demonstrated between those giving a history of interference and those who denied it.

Four hundred and twelve patients (77 per cent) were born in the United States, while 123 (23 per cent) were foreign born and the nativity of 2 was un-stated. Eighty-five per cent of those admitting induction were native born. The average education of the group was 7.5 years grade school. There were, however, significant differences in educational attainment between native born and foreign born, and between the "induced" and "spontaneous" groups. The native born were the better educated in all groups classified according to type of abortion. More of those who admitted induction, fewer of those who denied it, had attained high school than expected (Table II).

TABLE II. PATIENT'S STATEMENT OF TYPE OF ABORTION, BY EDUCATIONAL ATTAINMENT OF THE WOMAN AND BY NATIVITY

	CASES	%	COMPLETED GRADES											
			0	%	1-7	%	8	%	9-11	%	12	%	HIGH-ER	%
Induced	156	100	3	2	48	31	34	22	46	29	22	14	3	2
United States	132	85	2	2	34	26	32	24	42	32	19	14	3	2
Foreign	24	15	1	4	14	58	2	8	4	17	3	13		
Spontaneous	346	100	14	4	109	32	104	30	88	25	24	7	7	2
United States	258	75	1		69	27	85	33	75	29	21	8	7	3
Foreign	88	25	13	15	40	45	19	22	13	15	3	3		
Therapeutic	35	100	1	3	10	29	11	31	6	17	6	17	1	3
United States	24	69			5	21	8	33	5	21	5	21	1	4
Foreign	11	31	1	9	5	46	3	27	1	9	1	9		
Totals	537	100	18	3	167	31	149	28	140	26	52	10	11	2
United States	414	77	3	1	108	26	125	30	122	29	45	11	11	3
Foreign	123	23	15	12	59	48	24	19	18	15	7	6		

While considering nativity and education, we may as well turn to the childhood experience of these patients and to their present relations with their parents and siblings. These data, as has been said, are crude in the extreme and largely

influenced by convention. They are simply responses to the questions, "Did you have a happy childhood? Was it hard for your parents to supply you with necessities or did you have plenty? Do you still keep in touch with your family?" About two-thirds of all patients who were questioned (54 were not) answered unequivocally that their childhood had been happy and carefree, one-fifth had been frankly unhappy and suffered hardships, while the remainder reported a fairly happy childhood marred by the memory of some flaw such as poverty or unkindness on the part of father or stepmother. About half of the patients in each abortion category stated that they were in close touch with those of their families who were still alive and nearby. A fifth seldom saw their close relatives but were on good terms with them and kept up a correspondence. Eleven per cent of the spontaneous group stated that they had no close relatives living, but only 3 per cent of the induced were so bereft. On the other hand, twice as many (15 per cent) of the latter were on bad terms with their families. Only 8 per cent of the spontaneous mentioned quarrels and ill-feeling.

The sexual partners (husbands or otherwise) of about one-half (52 per cent) of these patients were employed in private enterprise. An additional 25 per cent were employed on relief projects or received regular government support of some sort. The remainder were either unemployed and not receiving relief (16 per cent) or else engaged in occupations unknown to the woman or uncommunicated to the examiner. There was no significant difference in the employment status of the male partners of the different abortion groups.

When the number of living children was correlated with the employment status of the man, the usual relationship was found: relief recipients had the largest families, unemployed nonrelief recipients next, and those employed in private enterprise the smallest. One hundred and ninety-one patients (36 per cent) had no living child; 39 per cent had 1 or 2 children and the remaining 25 per cent had 3 or more. The distribution of living children was approximately that of chance expectancy for the induced and spontaneous groups.

Thus, two important potential reasons for induction, too large a family and low economic status, did not characterize the induced abortion group in a manner significantly different from the spontaneous and therapeutic groups.

When, however, we turn from the employment of the father to that of the woman herself we find a wholly different state of affairs (Table III). Many

TABLE III. PATIENT'S STATEMENT OF TYPE OF ABORTION BY MARITAL STATUS AND BY WOMAN'S EMPLOYMENT*

(Selected Groups and All Cases)

	CASES	%	MARRIED	%	PREVIOUSLY MARRIED	%	SINGLE	%
Induced (mechanical)	52	100	28	100	7	100	17	100
Employed	26	50	6	21	5	71	15	88
Unemployed	2	4	--	--	--	--	2	12
Housewife	24	46	22	79	2	29	--	--
Spontaneous (true)	158	100	146	100	7	100	5	100
Employed	42	27	35	24	5	70	2	40
Unemployed	4	2	2	1	1	15	1	20
Housewife	112	71	109	75	1	15	2	40
All cases (except therapeutic)	502	100	362	100	74	100	65	100
Employed	158	31	79	22	41	55	38	46
Unemployed	36	7	7	2	17	22	12*	18
Housewife	308	62	277	76	16	23	15	46

*Including 6 students.

more than expected of the induced group were employed while many more of the spontaneous group were housewives. If the extreme groups, those who admitted mechanical induction and those who convincingly denied all interference, are compared, we find that the proportion of the former who were employed is twice

that of the latter, conversely 46 per cent of the former and 71 per cent of the latter were housewives. Here, too, marital status was largely responsible for the difference. Employed married women were somewhat less frequent in the induced group.

Overcrowding is often suggested as a potent cause for family limitation. Here again it must be remembered that the concept of overcrowding is relative. In our series the proportion of patients having more to those having less than two persons per room was practically the same in the induced and spontaneous groups. Thirty-six per cent of the induced group had more than 2 persons per room while this was true of 39 per cent of the spontaneous. In this study a child, even a small baby, was counted a person, hence the degree of crowding was less than would appear if "person-units" rather than persons were considered.

But persons-per-room does not tell the whole story. A married couple may share a single room and not feel particularly overcrowded, whereas 8 persons in a four-room flat may seriously interfere with each other's activities. Persons per household may be a more important factor conducive to induction. As will be shown later, the majority of patients in all categories stated that they considered two or three children an ideal number. Twenty per cent of the induced group had more than five persons in their household, while 14 per cent of the spontaneous group were overcrowded in this sense. However, this grouping is probably not valid as a significant number of patients considered 4 or 5 children desirable.

Although nearly two-thirds denied having taken any active step to rid themselves of the fetus, only a little over one-third denied that they had reasons for wishing interruption. Forty per cent declared that economic considerations made the birth of the child undesirable; 52, or one-third of those not living in wedlock, were influenced by shame. Thirty-six gave ill health as a reason, 24 of these belonging to the therapeutic group. Twenty-three had ideas of family planning and an equal number gave a variety of other causes. Only 2 of these mentioned fear of childbirth as a motive.

When asked if they would want a child, or an additional child, under more favorable conditions, the proportion just stated was reversed. A little over two-thirds (including half of those who were then hospitalized because of induced abortion) said "yes," while less than one-third said "no, they would have no such wish under any circumstances." This is at variance with the response of Pearce's English group. Only 25 per cent of these wished a child.

The average prior parity of the previously gravid group was 1.5, prior gravidity was 2.4; previous abortions, 0.8 (induced 0.3, spontaneous 0.5). One hundred and twenty-three patients had never given birth to a viable child and 191 had no living child at the time of the interview. But when asked what would be an ideal number of children under most favorable circumstances only 5 stated that an 0-child family would be desirable. The most popular size was the 2-child family which 204 patients preferred. Eighty-four per cent were in favor of 2- to 4-child families for those who were able to bear and care for them. In responding to this question which was, in effect, an invitation to build a castle in Spain, the induced and spontaneous groups showed no significant difference. The ideal families of negroes and whites were substantially the same.

The feelings expressed with regard to the current abortion were possibly largely influenced by convention. Two hundred and forty-eight patients expressed regret while 210 stated that they felt relief or satisfaction. Over half of the induced group gave voice to the latter state of mind, while 30 per cent of those who denied interference were also glad to be relieved of the prospect of a child. Twenty-three per cent of the induced said they regretted the termination of their pregnancy, as did 61 per cent of the spontaneous. Fourteen patients, 11 in the induced and 3 in the therapeutic group, expressed remorse. Twelve felt frightened by their condition.

Since unhappy marital adjustment is sometimes thought to play a part in influencing a woman to reject pregnancy, our patients were questioned with regard to their feelings about their sexual partners and coitus. These questions were answered in most cases without apparent reserve or resentment at the in-

vasion of privacy, but, as was said earlier, the answers are probably of little value. They are presented for what they may be worth. The observed data are closely in accord with chance expectancy, except for the high incidence of dislike for the partner (33 per cent), expressed by the single women in the induced group. Over 80 per cent of the married women stated that they loved their husbands. Seventy-three per cent of all patients frankly enjoyed coitus with their present partner. Eighty-seven per cent experienced orgasm with him though the majority qualified their statement by "sometimes" or "occasionally." Coital frequency varied greatly though the mode for all ages was "weekly or more but less than daily." Only 12 patients reported daily coitus. Three of these were in the 20 to 24 age group, 1 in the 25 to 29, 3 in the 30 to 34, and 1 in the 35 to 39. The other groups, "monthly but less than weekly" and "less than monthly," were similarly unaffected by age although age was shown to parallel duration of sexual experience closely.

One hundred and eighty-four of these patients (37 per cent) denied ever having heard of the existence of birth control clinics; 294 had heard of them from friends, relatives, doctors, nurses, or social agencies, but had never visited one. Only 53 (10 per cent) had been instructed in the diaphragm and jelly technique. Sixteen of the latter were using the method prior to this pregnancy, but few attributed conception to its failure. Most of the 16 confessed neglect to protect themselves on one or frequent occasions.

In contrast to the relatively small number who had availed themselves of medical counsel with regard to contraception, only 58 said that they or their husband were opposed to it on religious or other grounds, and 346 were using some method to prevent pregnancy at the time this conception was supposed to have occurred. An additional 24 had previously made contraceptive efforts but stated that they had suspended these for a planned pregnancy. One hundred and sixty-three denied any recent attempt to limit their fertility, but 20 of these acknowledged earlier contraception, leaving 143 who denied ever in their lives having used any method whatever to this end. Fifty-one of the noncontraceptors were primigravidas.

Of the contraceptive methods used by patients who had had experience with only one, douching was the most popular. Its use was reported by 90. Forty had relied on the condom and 31 on withdrawal. One hundred and forty-six, however, stated that they had used 2 or 3 of these (douche, condom, withdrawal) alternately or in combination. Only 39 reported the use of other methods (suppositories, pessaries, "the rhythm," etc.) immediately preceding this pregnancy.

All of the women were warned of the inadvisability of immediately becoming pregnant again regardless of their ultimate wish for a child. They were then questioned about their plans for avoiding this contingency. Two hundred and seventy-six (55 per cent) said they would like to be referred to Birth Control Clinics and were thereupon given definite written directions as to the address and hours of the nearest clinic to their homes. Nine were sterilized in connection with therapeutic hysterotomy. Sixty-nine (14 per cent) said they intended to abstain from coitus. Half of these were in the group who had induced abortion and most were single. One hundred and sixteen (23 per cent) intended to return to their former habit of contraception or noncontraception, and 5 per cent stated that they intended to resume their efforts to conceive immediately. Seven per cent were undecided as to their future course of action.

SUMMARY

The single, the white, the employed, the native American, the more highly educated woman was found significantly more frequently in the group who admitted induced abortion than among those who denied it. Women who felt a sense of economic pressure or shame, those who expressed no desire for a child, and those who had practiced contraception intensively howbeit ineffectively, were also significantly more frequent.

Religious affiliation, age, prior gravidity, prior parity, previous abortions, number of living children, enjoyment of coitus, feeling for sexual partner, employment of the latter, childhood experience, emotional relation to parents and siblings, number of siblings, number of persons per room, concept of size of ideal family, although perhaps influential in individual cases, did not show statistically significant differences in the groups characterized by admission or denial of interference.

The facts cited show that legal and religious disapproval mean little to the woman who is interested in limiting the size of her family. She uses such methods to prevent pregnancy as she and her partner know, and, when these fail, in many instances she takes drastic steps to rid herself of the fetus.

The most obvious first step toward reducing the incidence of abortion would be to provide the woman, who has recently given proof of the seriousness of her desire to limit her family, with more reliable methods of contraception than those she has previously tried. There would be fewer abortions, both induced and spontaneous, if every postabortal patient were routinely advised to refrain from immediate pregnancy, instructed in the way of carrying out this advice and fitted with a pessary (provided she desired it and this method were suitable in her case) at her follow-up visit to the gynecologic clinic.

Next in preference would be an intramural birth control clinic closely cooperating with the gynecologic and obstetric clinics.

Since political and religious opposition render both of these plans unfeasible in many hospitals, the next best thing would be to offer every patient of this type a definite reference to the birth control clinic most convenient to her home.

Popularization of the Aschheim-Zondek test and provision of this service at cost would reduce the incidence of "abortion" in the non-pregnant.

Although greater access to contraceptive advice and early diagnosis in amenorrhea would cut down abortions to some extent, this is only a stopgap approach to the problem.

The ultimate steps in the prevention of abortion are:

1. Preferential community services to families with children.
2. Maternity leave for employed women.
3. Social and economic aid to unmarried pregnant women and responsible agencies to care for and place illegitimate children.
4. Sex education at all levels correlated with instruction in child care and cultivation of an understanding of the values of parenthood. Many intelligent young people now enter upon life with the negative determination to avoid having too many children but without the positive inclination to have enough. The former position is easily acquired from observation of their elders and discussion among themselves; the latter requires systematic and intelligent presentation by competent teachers.

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WEIGHT CHANGES DURING PREGNANCY AND PUERPERIUM

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THE observation that gestation is accompanied by a progressive increase in weight of the mother, beyond that directly and indirectly attributable to the offspring, has continued to intrigue many investigators ever since Gassner first recorded this seemingly unnecessary weight gain. The association of excessive weight increase in the eclamptic syndrome, as shown by Zangemeister and several subsequent writers, adds further interest to this problem.

Of the numerous recent contributions that are of significance in connection with the findings in the present paper are those of Wodon, Evans, Siddall and Mack, McIlroy and Rodway, and Bray, to mention only some. Wodon directed attention to the importance of weight gain when expressed in terms of percentage of initial weight as contrasted with absolute weights. Bray emphasized the factors that do and those that do not influence weight gain. The English authors, as well as Siddall and Mack report the abnormal changes noted in certain of the toxemias of pregnancy.

As there appear to be marked differences in the published observations on gain and loss of weight associated with gestation and the puerperium in both normal and abnormal patients, we have deemed it advisable to correlate the weight changes during pregnancy and puerperium. It has been our routine practice, since September, 1932, to weigh all pregnant and puerperal patients at stated times, including those immediately before and after delivery.

Most of the previous investigations have dealt entirely with total weight changes. It seemed advisable that the normal curve for pregnancy should be determined so that deviations from the normal could be easily detected. Excessive weight gains have been recognized for a long time as indicative of toxemia, while early changes have not always been appreciated because of the lack of standard curves.

In this study we have also had the opportunity of studying the various types of toxemia. Since the investigation was begun before the new classification of toxemia, approved by a special subcommittee of the American Committee on Maternal Welfare, was adopted, an added opportunity was presented to compare the types of toxemia on the basis of weight change.

Moreover, we were particularly interested in devising some method of weight recording that would take into consideration the original weight of the patient. This we find exceedingly necessary, because too often the total weight gain is not evaluated in terms of the size of the patient. In other words, average weight gains mean little in the individual case.

DATA

The data are based on a study of 2,935 pregnancies. Many of the patients have been studied through two or more pregnancies. As is our routine practice, these patients were weighed at each antenatal visit, during labor, immediately following delivery, on discharge from the hospital (usually ten to twelve days post partum), and six weeks post partum. Patients are usually seen monthly during the first seven months of gestation, bi-weekly until the last month, when they are seen at weekly intervals. The weights during labor and immediately following delivery are obtained by the use of a special stretcher scale, which permits the patient to be weighed without getting up. Obviously in some of these patients, one or more of these weights were not obtained for various reasons.

In addition, 35 patients were studied daily for a week or more prior to delivery. Most of these patients were in the hospital because of various complications of pregnancy, although some had perfectly normal pregnancies.

The diagnosis of toxemia was based on a complete study which included symptomatology, blood pressure, urine examination, kidney function tests (phenol-sulfonephthalein and urea clearance), blood chemistry, and eye ground examinations. Whenever possible correlation with the new classification will be made. Obviously, the period of observation varied in these patients. Only seven patients were first seen in their sixth week of gestation. The number seen in successive weeks progressively increased until the thirtieth to thirty-second week when they decreased because of premature delivery.

The results will be presented in different groups, namely, normal pregnancy, twin pregnancies, and the various types of toxemia. In all cases the weekly weight gains were calibrated from the recorded data, i.e., it was assumed that the weight gain between two periods of observation was uniform throughout that interval. In the cases of toxemia, this might not have been true if the interval between observations was too long. Moreover, the percentage increase or loss was calculated in each case. This will be discussed later.

Normal Pregnancy.—The weight changes in 2,502 normal pregnancies were studied. The usual weight given by these patients was an average of 58.3 kg. It is significant to note that the average usual weight for primiparas (1,227 cases) was 57.3 kg., whereas that for multiparas (1,097 cases) was 60.5 kg. This same difference obtained throughout the subsequent weights. Consequently, no difference in weight changes was noted between the multipara and primipara throughout pregnancy or the puerperium.

In Fig. 1 is represented the average weight changes during pregnancy and the puerperium in the 2,502 normal pregnancies. As seen in the chart, a few of the patients went beyond the fortieth week of gestation. This is represented by the dotted line. Undoubtedly some of these were due to miscalculation of the last menstrual period. In another study the difference in the weight of the baby in respect to the period of gestation will be presented.

The average weight gain up to the fortieth week of pregnancy was 13.96 kg. This is slightly higher than figures given by other investigators, but may be due to difference in diets, as most of our patients included in their diet one quart of milk per day. Also this gain is calculated from the sixth to the fortieth week and not from the usual weight given by the patient.

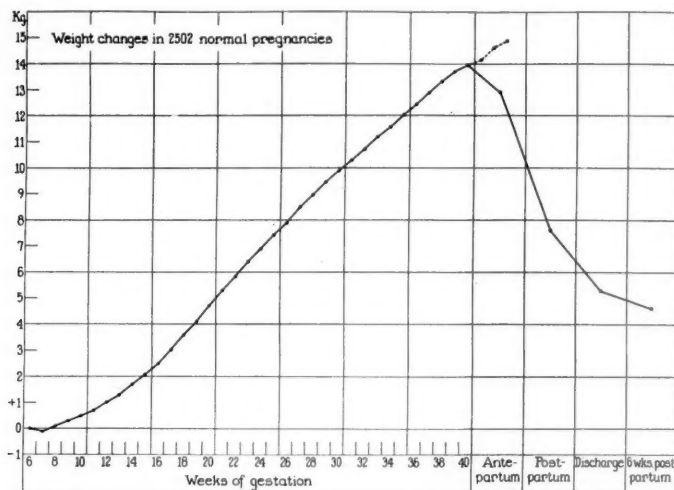


Fig. 1.—Average weight changes during normal pregnancy and puerperium.

During the interval between the last visit to the dispensary and the onset of labor (usually seven to ten days), there was an average loss of 1.11 kg. For convenience, labor is represented in the chart as starting at the fortieth week of gestation. This, of course, was not true in all cases but the change in weight was calculated as the difference between the weight in labor and the last weight in the dispensary. This drop in weight was substantiated by the 35 cases which were followed daily in the hospital.

The average weight loss during delivery was 5.34 kg. If anything, the multiparas lost slightly less than the primiparas. During the first ten days of the puerperium (discharge), there was an additional loss of 2.3 kg. A further loss of 0.68 kg. was sustained until the six weeks post-partum visit. The average weight for six weeks post partum was 60.76 kg., the average for the primiparas being 59.47 kg. and that for the multiparas 62.20 kg., or approximately the same difference as in the usual or nonpregnant weight. They were still above the weight at the onset of pregnancy but were close to the usual weight of 60.52 kg. as given by the multiparas. As a rule, it can be said that the primipara does not return to her usual weight.

Throughout the study of these cases it was noted that the changes in weight were proportional to the original weight of the patient. The heavier the patient at the onset of pregnancy, the more marked the increase in weight. Consequently the weight changes per se are of slight significance unless the original weight of the patient is taken into consideration. This is important, because many heavy patients are unnecessarily placed on restricted diets and treated for toxemia because of what appears to be excessive weight gain, while abnormal weight gain is overlooked in small individuals.

For this reason, it was felt that the weight changes should be calibrated on the basis of percentage gain or loss, so that comparisons could be made. The percentage change for each week was, therefore, calibrated for the above patients. These data

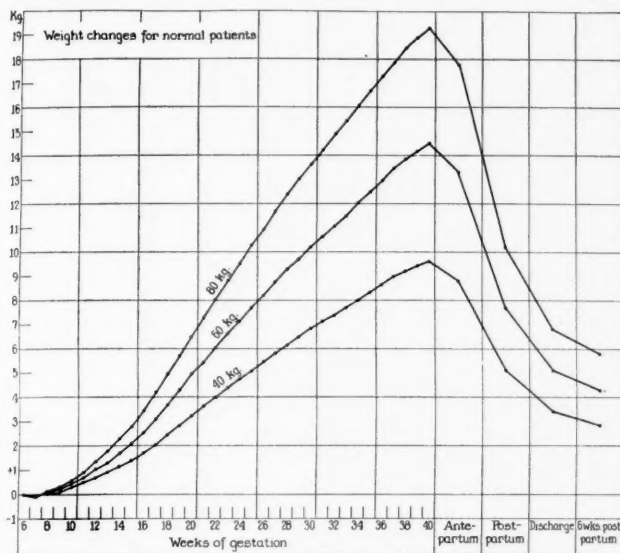


Fig. 2.—Normal weight changes for patients weighing 40, 60, and 80 kilograms.

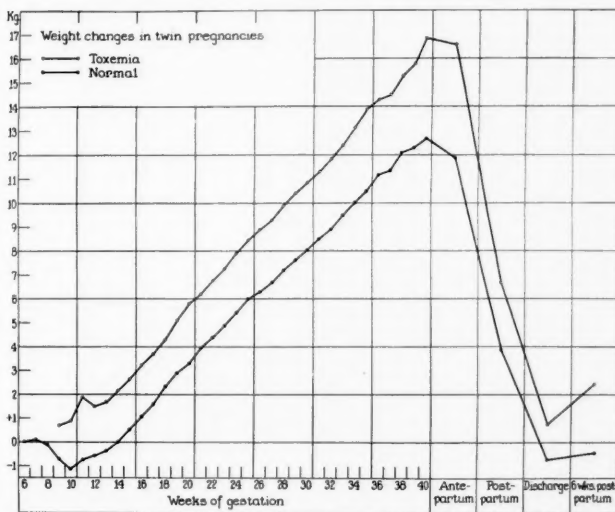


Fig. 3.—Weight changes in twin pregnancy for patients weighing 60 kilograms.

can be seen in the first column of Table I. The percentage increase through the fortieth week of pregnancy was 24.10 per cent. The percentage loss during delivery and the puerperium is also noted in Table I. On this basis, the normal curves for patients weighing 40, 60, and 80 kg., respectively, at six weeks gestation, were constructed and are shown in Fig. 2. Such a chart has now been adapted for use in the antenatal record, so that any changes from normal can be easily detected. For practical purposes the usual weight given by the patient can be regarded as the sixth week weight, and the first recorded weight is placed in its proper spacing. Subsequent changes should conform to the normal curves.

TABLE I. WEIGHT CHANGES

WK.	NORMAL				TWINS—NORMAL		TWINS—TOXEMIA	
	% CHANGE	TOTAL WEIGHT	TOTAL WEIGHT	TOTAL WEIGHT	% CHANGE	TOTAL WEIGHT	% CHANGE	TOTAL WEIGHT
6		40.00	60.00	80.00		60.00		60.00
7	-0.12	39.35	59.92	79.90	0.29	60.17		
8	+0.26	40.04	60.07	80.10	-0.48	59.88		
9	0.323	40.17	60.26	80.35	-0.48	59.59	1.27	60.76
10	0.382	40.32	60.49	80.65	-0.69	59.17	0.37	60.98
11	0.404	40.48	60.73	80.97	+0.61	59.53	1.61	61.96
12	0.481	40.67	61.02	81.35	0.21	59.65	-0.85	61.43
13	0.552	40.89	61.35	81.79	0.32	59.84	0.37	61.65
14	0.574	41.12	61.70	82.25	0.32	60.03	0.72	62.09
15	0.674	41.39	62.11	82.80	0.92	60.58	0.91	62.65
16	0.781	41.71	62.59	83.44	0.95	61.15	0.91	63.22
17	0.863	42.06	63.13	84.16	0.95	61.73	0.89	63.78
18	0.905	42.44	63.70	84.92	1.01	62.35	0.91	64.36
19	0.934	42.84	64.29	85.71	0.83	62.86	1.22	65.14
20	0.935	43.24	64.89	86.51	0.77	63.34	0.98	65.77
21	0.905	43.63	65.47	87.29	0.85	63.87	0.73	66.25
22	0.889	44.02	66.05	88.06	0.84	64.40	0.81	66.78
23	0.879	44.40	66.63	88.83	0.78	64.90	0.84	67.34
24	0.830	44.77	67.18	89.56	0.80	65.41	0.79	67.87
25	0.799	45.12	67.71	90.27	0.74	65.89	0.85	68.44
26	0.778	45.47	68.23	90.97	0.65	66.31	0.61	68.85
27	0.830	45.84	68.79	91.72	0.70	66.77	0.75	69.36
28	0.728	46.18	69.29	92.38	0.66	67.21	0.77	69.89
29	0.715	46.51	69.78	93.04	0.63	67.63	0.76	70.42
30	0.658	46.82	70.23	93.65	0.69	68.09	0.62	70.85
31	0.652	47.12	70.68	94.26	0.57	68.47	0.71	71.35
32	0.628	47.41	71.12	94.85	0.66	68.92	0.52	71.72
33	0.658	47.72	71.58	95.47	0.84	69.49	1.00	72.43
34	0.664	48.03	72.05	96.10	0.77	70.02	1.04	73.18
35	0.669	48.35	72.53	96.74	0.64	70.46	1.04	73.94
36	0.615	48.64	72.97	97.33	0.90	71.09	0.47	74.28
37	0.639	48.95	73.43	97.95	0.42	71.38	0.26	74.47
38	0.566	49.22	73.84	98.50	1.08	72.15	1.04	75.24
39	0.424	49.42	74.15	98.91	0.26	72.33	0.77	75.81
40	0.449	49.64	74.48	99.35	0.49	72.68	1.32	76.81
Total	24.10				21.13		28.01	
Labor	-1.58	48.85	73.30	97.78	-1.08	71.89	-0.24	76.62
Delivery	-7.74	45.07	67.62	90.21	11.02	63.96	-12.86	66.76
Discharge	-3.77	43.37	65.07	86.80	-6.92	59.53	-9.15	60.65
6 Wk. P.P.	-1.11	42.88	64.34	85.83	+0.46	59.80	+2.89	62.40

The data to be presented for abnormal pregnancies have all been calculated according to percentage change and, for purpose of comparison, have been standardized for patients weighing 60 kg. at six weeks of gestation.

Twin Pregnancies.—Weight studies on 131 twin pregnancies were conducted. Of these, 95 were in normal pregnancies, and 36 in patients with one or another type of toxemia. The weight changes (standardized) are seen in Fig. 3, and the percentage changes are recorded in Table I. The weight gain for normal twin pregnancies was less than normal, namely 21.13 per cent instead of 24.10 per cent. This seems to be due to excessive loss during the early weeks of pregnancy. As expected, the loss during delivery is greater than in single pregnancy. The loss during the first ten days of the puerperium is also excessive, 6.9 per cent or 4.4 kg. Following this, there is an increase during the last five weeks of the puerperium.

The increase in weight in the patients with toxemia was greater than normal, 28.01 per cent, as contrasted with 24.10 per cent for the normal. This increase seems to be concentrated during the early weeks of pregnancy, otherwise the curve is

DURING PREGNANCY AND PUERPERIUM

CHRONIC NEPHRITIS		UNCLASSIFIED		LOW RESERVE KIDNEY		PRE-ECLAMPSIA		ECLAMPSIA	
% CHANGE	TOTAL WEIGHT	% CHANGE	TOTAL WEIGHT	% CHANGE	TOTAL WEIGHT	% CHANGE	TOTAL WEIGHT	% CHANGE	TOTAL WEIGHT
	60.00		60.00		60.00		60.00		60.00
		0.24	60.14	+0.37	60.22				60.00
	60.00	0.10	60.20	-0.20	60.09	0.59	60.35		60.00
-1.20	59.28	0.15	60.29	0.83	60.58	0.59	60.70		60.00
-1.23	58.55	0.25	60.44	0.76	61.04	0.50	61.00		60.00
-0.59	58.20	0.25	60.59	0.60	61.40	0.64	61.39	0.25	60.15
+1.09	58.83	0.49	60.88	0.61	61.77	0.68	61.80	0.47	60.43
1.08	59.46	0.72	61.31	0.65	62.17	0.73	62.25	0.79	60.90
1.07	60.09	0.50	61.61	0.67	62.58	0.73	62.70	0.97	61.49
0.68	60.49	0.66	62.01	0.75	63.04	0.82	63.21	0.96	62.08
0.68	60.90	0.73	62.46	0.81	63.55	0.65	63.62	0.93	62.65
0.72	61.33	0.72	62.90	0.87	64.10	0.51	63.94	0.89	63.20
0.72	61.77	0.72	63.35	0.90	64.67	0.67	64.36	0.69	63.63
0.57	62.12	0.84	63.88	0.89	65.24	0.78	64.86	0.59	64.00
0.42	62.38	0.75	63.35	0.92	65.84	0.90	65.44	0.92	64.58
0.54	62.71	0.72	64.81	0.88	66.41	1.00	66.09	0.87	65.14
0.56	63.04	0.79	65.32	0.84	66.96	1.03	66.77	0.99	65.78
0.64	64.14	0.79	65.83	0.83	67.51	0.32	66.98	1.01	66.44
0.42	64.40	0.65	66.25	0.85	68.08	0.48	67.30	0.97	67.08
0.50	64.72	0.66	66.68	0.88	68.67	0.79	67.83	0.95	67.71
0.40	64.97	0.63	67.10	0.72	69.16	0.98	68.49	1.10	68.45
0.58	65.34	0.56	67.47	0.75	69.67	1.05	69.20	1.10	69.20
0.62	65.74	0.64	67.90	0.82	70.24	0.76	69.72	1.04	69.91
0.43	66.02	0.64	68.33	0.70	70.73	0.74	70.23	1.22	70.76
0.51	66.35	0.70	68.80	0.58	71.14	0.91	70.86	0.69	71.24
0.50	66.68	0.73	69.30	0.67	71.61	0.86	71.46	0.85	71.84
0.38	66.93	0.50	69.64	0.73	72.13	0.74	71.98	1.28	72.75
0.49	67.25	0.53	70.00	0.74	72.66	1.21	72.85	0.87	73.38
0.68	67.70	0.52	70.36	0.74	73.19	0.61	73.29	0.92	74.05
0.29	67.89	0.60	70.78	0.72	73.71	0.55	73.69	0.32	74.28
0.80	68.43	0.36	71.03	0.51	74.08	1.03	74.44	0.46	74.62
0.09	68.49	--	71.03	0.31	74.30	0.25	74.62	1.68	75.87
	68.49	0.24	71.20	0.41	74.68	0.64	75.09	-0.23	75.69
14.15		18.66		24.46		25.15		26.15	
-1.99	67.12	-4.19	68.21	-3.41	72.13	-2.51	73.20	+1.119	76.53
-5.24	63.60	-7.22	63.28	-8.96	65.66	-7.16	67.95	-12.69	66.81
-5.73	59.95	-1.87	62.09	-2.78	63.83	-7.23	63.03	-6.29	62.60
-2.20	58.63	+2.07	63.37	+2.98	64.02	+1.09	63.71	+0.75	63.07

parallel with that of normal twin pregnancies. In these patients, there was only a slight weight loss before labor, but the weight loss during delivery and early puerperium was excessive, 12.86 per cent and 9.15 per cent or 9.4 kg., and 5.8 kg., respectively. The weight gain during the last five weeks of the puerperium in all the twin pregnancies simulates the cases with toxemia, as will be shown presently.

TOXEMIA

The various types of toxemia will be discussed separately. As stated above, reference to the new classification will be made whenever possible.

Chronic Nephritis.—There were 25 patients with definite chronic nephritis, showing the typical changes in kidney function tests and eye ground findings. As expected, their weight gain was below normal, namely 14.50 per cent. There was excessive loss during the early weeks of pregnancy as can be seen in Fig. 4, as compared with the normal curve. Their loss during delivery was below normal, due un-

doubtedly to small babies and premature labors. There was a steady loss after delivery so that even at six weeks post partum, the weight was below the original weight. As far as weight was concerned, these patients were definitely worse after the pregnancy. Some of this loss may have been due to edema. These cases would now be classified under renal disease.

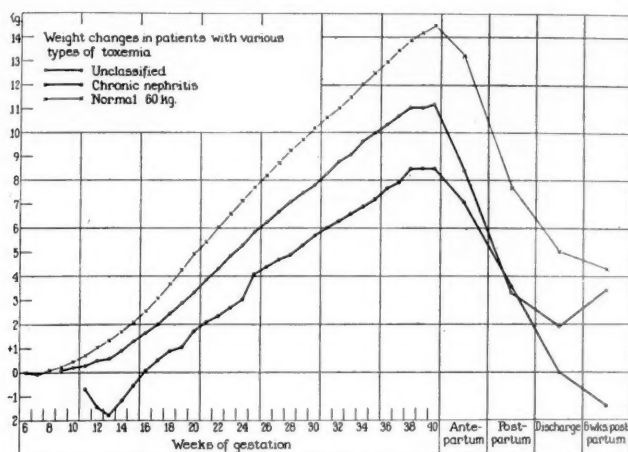


Fig. 4.—Weight changes in certain types of toxemia of pregnancy for patients weighing 60 kilograms.

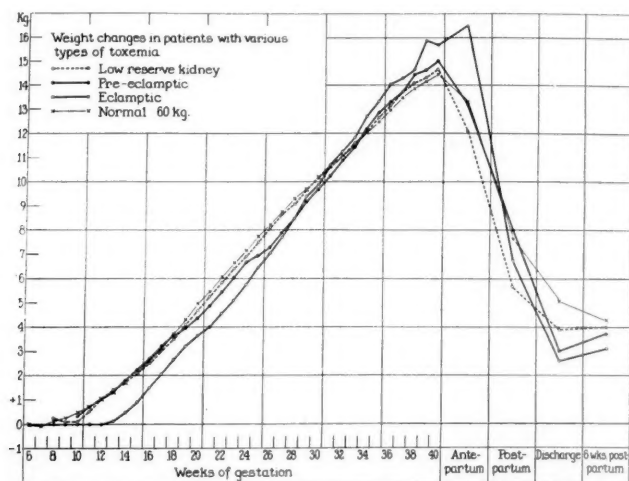


Fig. 5.—Weight changes in certain types of toxemia of pregnancy for patients weighing 60 kilograms.

Unclassified Toxemia.—There were 70 patients with unclassified toxemia in this study. In this category, we have included patients in whom a definite diagnosis could not be made. However, it has been our experience, that many of these show definite signs of chronic nephritis in subsequent pregnancies. Also included in this group are many cases which we would now designate hypertensive disease. No definite kidney impairment was detected in any of them.

The weight curve is between normal and that for the chronic nephritic group. Their weight gain was 18.66 per cent. They showed a greater loss just before labor, although the loss during delivery was not excessive, as can be seen in Fig. 4. There was some gain in weight during the latter part of the puerperium. In contrast to

other forms of toxemia both the chronic nephritis and the unclassified group are definitely below the normal curve.

Low Reserve Kidney Toxemia.—The study included 149 cases of low reserve kidney. This group is made up largely of cases now designated as mild pre-eclampsia. A few cases of hypertensive disease would also be included. It should also be remembered in discussing these patients with toxemia that no sharp changes are noted in Fig. 5. This is due to the fact that they are composite charts and do not represent individual cases. The marked changes corresponding to the episode of severe illness varied as to its time of onset; consequently the curve is more uniform than expected. However, we were particularly interested in studying any possible significant change, even prior to the sudden increase in weight. As seen in Fig. 5, all of the toxemias represented in the chart are above the normal curve, except for the early weeks of pregnancy. The types of curve are similar and vary only in degree, which would tend to place them in one type of toxemia. The patients with low

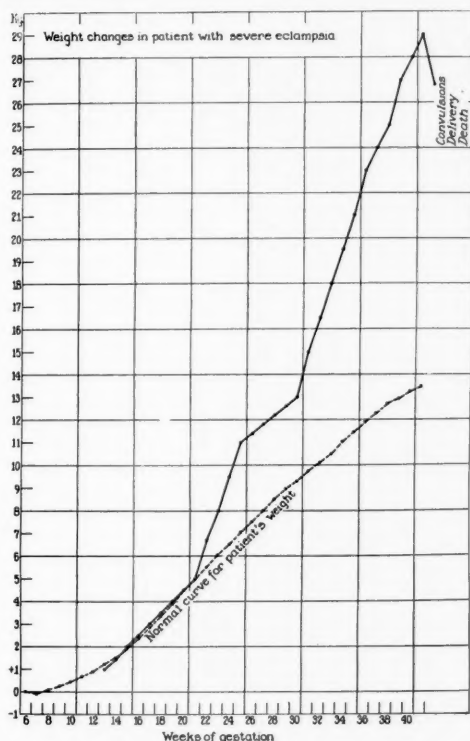


Fig. 6.—Comparison of the weight changes in a patient with eclampsia with the normal curve for her weight.

reserve kidney gained 24.46 per cent or slightly above normal. Their loss before labor, delivery, and puerperium is quite marked, and the gain during the late puerperium is definite. This conforms with the pre-eclamptic and eclamptic cases.

Pre-eclampsia.—Weight changes in pre-eclampsia were studied in 28 patients. These cases are definitely those which we would now call severe pre-eclampsia. The changes are practically those mentioned under low reserve kidney. The total gain was 25.15 per cent. They showed more loss in weight during the early puerperium than during delivery. In this respect they simulate the patients with eclampsia. The loss before delivery is less but is compensated for during the early puerperium.

Eclampsia.—Thirty cases of definitely proved eclampsia are included in this study. The changes are similar to those already mentioned, except to a greater degree. It is significant to note that there was no weight gain during the early

weeks of pregnancy. This may prove to be a helpful sign in early diagnosis. The total gain was 26.15 per cent. There was an additional gain of 1.1 per cent just before labor. It is during this period that the illness is usually most severe. The loss during delivery is greater, as is also the loss during the early puerperium. The characteristic gain during the late puerperium is noted.

In both the eclamptic and pre-eclamptic patients, individual cases showed rather sudden increases in weight. In Fig. 6, is shown the weight curve of a patient with severe eclampsia, who died shortly after delivery. Autopsy findings confirmed the diagnosis. Convulsions preceded delivery by one day. There had been no marked symptoms prior to this. Contrasted to it is the normal weight curve for a patient of her weight. It can be seen that there were two episodes of increase in weight, one of these early in pregnancy and a second increase in rate of gain about the thirtieth week of pregnancy. Both of these offered early diagnosis. Unfortunately she was not admitted until the day before delivery, and the disease was so overwhelming that delivery had no beneficial effect. The chart does show the importance of recording the weight changes graphically in contrast to normal curves. Early detection of abnormalities can then be made, and it is for that reason that the chart in Fig. 2 is presented for routine use during the antenatal period.

DISCUSSION

The weight gain during pregnancy is out of proportion to the weight of the products of conception, which approximately account for one-third of the total gain. This excess is undoubtedly mainly due to fluid retention not only in the circulation but also in the tissues. This would indicate that approximately 16 per cent weight increase over the non-pregnant weight is due to fluid. Experiments have already shown that there is about 20 per cent dilution of blood due to hydremia, and it is reasonable to assume that there is an equivalent dilution of the tissue fluids. This is substantiated by the rapid loss during the early puerperium, at a time when the urinary output far exceeds the liquid intake. There is only a slight drop in weight during the late puerperium and most of this is probably accounted for by the involution of the uterus. The loss during delivery (5.34 kg.) can easily be accounted for by the weight of the baby, placenta, amniotic fluid, and blood loss. Moreover, the marked loss in weight following delivery in the patients with toxemia also seems to indicate that the normal process has been accentuated. In these cases we are certain that the water retention is not in the circulating blood (since studies have shown concentration of the blood elements), and yet many of these patients show practically no generalized edema. The atonic and flaccid condition of the tissues also indicates increased tissue fluid.

SUMMARY AND CONCLUSIONS

A study of the weight changes in 2,935 pregnancies is presented. The average curve for normal pregnancy is shown. Standardized curves of percentage change in weight are presented. This offers an easy method of recording weight changes which allows early recognition of abnormalities and permits comparison of cases. Twin pregnancies as well as the various types of toxemia were studied.

The following conclusions can be drawn.

1. Average weight increase from the sixth to fortieth week of pregnancy was 13.9 kg., or 24.10 per cent.

2. The average loss during the week prior to labor was 1.11 kg., or 1.58 per cent.
3. The loss during delivery was 5.35 kg., or 7.74 per cent.
4. Average loss during the first ten days of the puerperium was 2.30 kg., or 3.77 per cent.
5. Further loss of 0.68 kg., or 1.11 per cent, was sustained during the last five weeks of the puerperium.
6. Primiparas as a rule do not return to their original weight following pregnancy.
7. There is no difference in weight changes between the primipara and the multipara.
8. The weight gain in twin pregnancy is not excessive, but the loss during delivery and puerperium is definitely increased.
9. Chronic nephritis and unclassified toxemia show poor weight gain.
10. Low reserve kidney, pre-eclampsia, and eclampsia show similar weight changes, differing only in degree. The total gain is increased, but the loss during delivery and puerperium is excessive. This study would tend to include the three forms under one type.
11. Lack of gain during early pregnancy seems to be a significant sign in the eclamptic toxemias.
12. Weight changes seem to substantiate the new classification of toxemias.
13. The specific weight changes for any woman during normal gestation are proportional to her nonpregnant weight, and for this reason it is essential that weight changes be plotted in such a manner that they may be compared with the normal curves. This may be done by recording the weight changes against the normal weight curves which we have presented for 40, 60, and 80 kg., respectively.

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Perrenoud, J. P.: **The Frequency of Double Follicular Rupture. The Duration of the Involution of the Corpus Luteum**, *Rev. franç. de gynéc. et d'obst.* 34: 299, 1939.

The autopsy studies of Perrenoud revealed that double rupture of ovarian follicles is not frequent in spite of Samuels' contentions. It occurs about once in every six or eight ovulations. The author found evidence of double ovulation five times in 41 autopsy cases and once in operative cases.

The involution of the corpus luteum usually ends in eight to ten weeks but sometimes it takes much longer when there is no formation of new corpora lutea. The persistence of these old corpora lutea, contrasted often with atrophy of all the organs in general and of the genital tract in particular, indicates that they have one or more important functions in addition to their influence on the uterine mucosa.

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A CLINICAL STUDY OF STILBESTROL*

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IN 1934 Cook, Dodds, Hewett, and Lawson reported on the estrogenic activity of some condensed-ring compounds. Following this work, in 1938 Dodds, Goldberg, Lawson, and Robinson described the synthesis of dihydroxydiethyl stilbene, a chemical with marked estrogenic activity. They gave the name of stilbestrol to this new organic compound. Although a most potent estrogen, it is not related chemically nor in any other way to the naturally occurring estrogens. Careful biologic standardization indicates that 1 mg. of this new drug is equivalent in action to 25,000 international units of estrone. Other derivatives of stilbene have varying estrogenic action, but stilbestrol is the most potent of the group. Dodds and his associates, as well as a number of other investigators, have studied the estrogenic action of stilbestrol. These reports indicate that this organic drug will reproduce all the physiologic changes that can be induced by the natural estrogens.

The toxicity of the drug has been studied in laboratory animals and varies widely. Rabbits withstood 30 mg. per kilogram administered intravenously, although cats succumbed to this dosage. Guinea pigs are unusually tolerant of the drug, for they showed no effects from huge doses of 200 mg. per kilo. of body weight. Experiments with the prolonged administration of the drug to laboratory animals are still under way. It is exceedingly important to determine the effect of small and moderate amounts administered at frequent intervals over long periods of time for this mode of administration more nearly simulates the clinical use of the drug.

Loeser administered large amounts of stilbestrol to rats and at autopsy noted changes in the liver, kidneys, and adrenal which he interpreted as manifestations of toxicity. The total dosage that these animals received is not at all comparable to the amounts necessary in the clinical application of this new estrogen. Engle and Crafts recently administered from one to 200 mg. of stilbestrol orally and intramuscularly to monkeys and noted no signs of illness or toxicity. Many other investigators have made careful laboratory and clinical observations for evidence of toxicity with entirely negative results.

When stilbestrol was first administered to patients, nausea with or without vomiting occurred frequently. This gastrointestinal disturbance followed parenteral as well as oral administration. Enteric coating for oral tablets did not eliminate the nausea. In an effort to eradicate this undesirable feature, the drug was given in varying amounts and at different times of the day. It was found that most patients could take a

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1 mg. tablet at bedtime without any discomfort. In most patients this amount is sufficient to produce the desired estrogenic action. Larger daily doses of stilbestrol increased the incidence of a gastrointestinal upset, although many patients can tolerate as much as 25 mg. daily without the slightest discomfort. Experiments are under way which we hope will shed some light on the cause and the mechanism of the nausea induced by this medication.

No other undesirable reactions have occurred in the patients on stilbestrol medication. Frequent blood pressure readings revealed no abnormal variations. Urine examinations were consistently negative. There were no evidences of liver damage that could be elicited by careful observation and by the usual tests for impaired function. No dermatoses appeared on any of the women under observation.

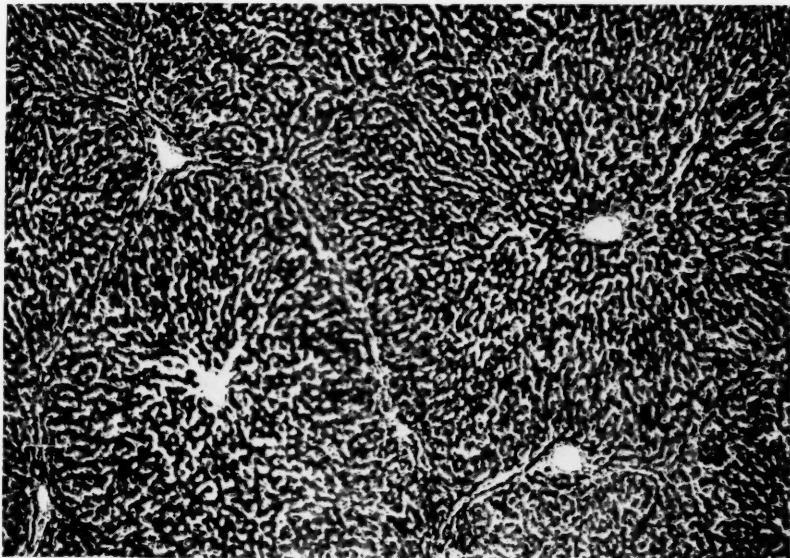


Fig. 1.—A histologic section of the liver of a patient who received 1,125 mg. of stilbestrol in forty-five days, showing no unusual fatty metamorphosis.

It was deemed advisable to make an attempt to evaluate the effects of prolonged administration of stilbestrol in women. Three patients with extensive terminal malignancies were given 10 to 25 mg. of stilbestrol daily. They tolerated the drug exceedingly well and it did not produce undesirable symptoms. These women received a total dosage of 250 mg. in ten days, 350 mg. in thirty-five days, and 1125 mg. in forty-five days, respectively. At autopsy the livers, kidneys, and adrenals were carefully studied (Fig. 1). These organs exhibited no more than the usual changes seen in patients who die after a prolonged illness such as the result of a malignancy. No gross fatty metamorphoses were present in any of these organs. These studies, while not conclusive in any way, confirm the belief that stilbestrol in the moderate doses necessary for clinical administration is not a toxic drug.

Stilbestrol can be administered subcutaneously, orally, and per vaginam. The most striking characteristic is the efficacy of the oral administration of this drug. Leighty and Wick have just reported that whereas it requires 25 to 30 times the amount of estrone administered orally to reproduce the action of subcutaneous administration, it requires only six times the amount of stilbestrol. Stilbestrol is at least five times as efficacious as the natural estrogen, estrone, when administered orally. The oral administration of this chemical has a prolonged estrogenic action. This property of the drug makes it particularly appealing for use by the clinician. The daily oral administration of a small amount of stilbestrol will maintain a constant blood level of estrin, thereby more nearly duplicating normal conditions. The failure of estrogenic therapy in the past has been due in part to inadequate amounts of the natural estrogens as well as to the difficulties inherent in the mode of administration necessary to provide a constant and adequate blood level.

The clinical use of stilbestrol is indicated in those conditions in which estrogenic medication is desirable. Although our observations have been under way about a year, it has been possible to study only a few conditions carefully.

MENOPAUSE

The treatment of the menopause has improved immeasurably since the introduction of endocrinal therapy. Most patients can be given some measure of relief, but there are still many instances where present-day treatment has not provided effective therapy. The most important reason for therapeutic failure is the fact that we do not understand the physiologic mechanism of the climacteric. Obviously, the symptoms of the menopause are brought on by the removal of ovarian influence, naturally or artificially.

The therapy of the menopause by means of estrogens is not considered entirely one of replacement. The gonadotropic principle in the urine is increased following the cessation of cyclic activity in the ovaries. This gonadotropic principle is almost a pure follicle-stimulating substance. Many investigators believe that estrogenic therapy produces its favorable action on the menopausal symptoms by a suppression of gonadotropic hormone production. Heller and Heller recently demonstrated the fact that although estrogens alleviate vasomotor symptoms they fail concurrently to reduce gonadotropic production, for the concentration of this material in the urine does not diminish appreciably under therapy.

The natural estrogens have been used extensively in the therapy of the menopause. In most instances these are administered in oily vehicles intramuscularly or subcutaneously. More recently estriol has been used for oral administration. Estradiol is the most effective and estrone the least effective of the natural estrogens. The amount of the hormone administered varies with the individual. Usually from 2,500 to 5,000 international units a week provides some relief, although in some instances as much as 10,000 to 50,000 units are necessary. The duration of the treatment is adapted to individual needs. Such a therapeutic regime provides moderate relief to the majority of patients; no relief

to a considerable number. The mode of administration, the difficulty in maintaining a constant estrogenic level, and the expense of high dosages and prolonged administration have worked to defeat the efficacy of the endocrine treatment of the climacteric.

In evaluating the results of any therapeutic regime in the treatment of the menopause, criteria are exceedingly difficult to select. The climacteric presents such a bizarre picture that few symptoms occur with sufficient regularity to be useful in evaluating results. It is this kaleidoscopic clinical picture that has resulted in the use of many different forms of therapy with good and bad results as the case may be. The most clear-cut symptomatology of the menopause develops in a young woman who has been subjected to an artificial climacteric as a result of surgery or radiation. Here the vasomotor changes predominate. Nervous phenomena and headaches are of secondary importance. Most of these manifestations come on a month to several weeks or more after the cessation of ovarian function. The hot flushes can be used as criteria of the climacteric, for they are pathognomonic. Their amelioration or disappearance is an indication of successful therapy. Nervous phenomena and headaches are less consistent end points.

MATERIAL

A selected group of women in the menopause were placed on stilbestrol therapy. These patients had been on careful observation for periods of from three to ten months. They had returned every four weeks for a careful study. The usual pelvic examinations were supplemented by vaginal smears, vaginal and endometrial biopsies, complete blood studies, blood pressure readings, and examinations of the urine. Notations of any untoward complaints or symptoms were made.

Of the 100 women thus studied the menopause had a natural onset in 46, whereas in 54 women it was artificially induced by surgery or radiation. Nine of the women had radiation for the therapy of some pathologic condition. The age of onset of the menopause varied: 16 per cent from 30 to 40 years, 30 per cent from 41 to 45 years, 37 per cent from 46 to 50 years, and 17 per cent from 51 years and over.

Early in this clinical investigation each patient received 5 mg. of stilbestrol daily but this amount was soon reduced to 1 mg. a day, taken at bedtime. It was found that this quantity was sufficient to control all the symptoms of the menopause. About 20 per cent of the women who were receiving 5 mg. of stilbestrol daily complained of nausea with or without vomiting or an uneasy and uncomfortable sensation in the abdomen. When the daily dose was reduced to 1 mg., most of these women could tolerate the medication without any apparent discomfort. In only three instances did the patient object to taking the medication, because the morning nausea and the upset feeling persisted. In a few more instances the patients experienced some nausea for several days after the institution of treatment, but this quickly subsided and did not return.

Ninety-three of the 100 women placed on stilbestrol were completely relieved of their menopausal symptoms. The hot flushes with their concomitant chilly sensations and uncomfortable sweats often disappeared within seventy-two hours following the onset of treatment. The relief was so rapid and so complete that many women expressed amazement at the result. Although the hot flushes were used as criteria of the menopause and their disappearance as a guide to effective treatment, other characteristic menopausal symptoms likewise disappeared. Headaches and the peculiar tenseness that develops at the back of the head and neck muscles disappeared or were improved. Nervous manifestations and the hyperexcitability and irritability characteristic of the climacteric were relieved. The mental depression that often develops was likewise improved. Many patients

volunteered the fact that they felt better than they had in years, that they experienced a sense of well-being and a renewed enthusiasm for living, that they were once more viewing life and its many problems and responsibilities through rose-colored glasses.

In 4 women, only partial relief of menopausal symptoms was obtained. Two of these women took the drug intermittently. In these women the characteristic flushes disappeared completely, but multitudinous complaints persisted and interfered with a complete recovery. These may or may not have been associated with the climacteric.

Twelve women in the group had been treated with the natural estrogens by parenteral administration. For varying periods some of these patients had fairly complete relief from symptoms. The majority of them had little relief but continued on treatment, because it was the best therapy we had to offer. Many a conscientious worker has often questioned how much of the therapeutic result was due to the hypodermic rather than to the estrogen administered. We must admit that it was exceedingly difficult to substitute oral medication for the hypodermic injections, but the striking improvement that followed stilbestrol convinced all but one woman in a very few days that the change in therapy was a desirable one. These women were rapidly freed of all their flushes, and of most of the other concomitant complaints.

There are no definite criteria to indicate the end of the menopause, for this physiologic episode varies considerably in length. When it occurs naturally, it may last from two to four years, for there is no sudden cessation but a gradual waning of ovarian activity. The artificial menopause is induced abruptly following surgery or radiation so that it is shorter in duration, rarely lasting longer than two years. The age of the individual likewise influences the length of the menopause and the severity of the symptoms. Young women are more likely to experience a stormy transitional period (Tables I and II). Medication must be continued until the symptoms begin to wane or disappear. After several months of medication the drug can be reduced, administering 0.5 mg. daily or 1 mg. every other day. In the event that symptoms return, the daily dose can again be increased. It is important to maintain continuous administration of stilbestrol, gradually reducing the amount but not interrupting its administration. A sudden cessation of

TABLE I. ARTIFICIAL MENOPAUSE, K. D. (No. 215115), AGED 49 YEARS

July 6, 1939: Incomplete hysterectomy, bilateral salpingo-oophorectomy (huge fibromyomas).

July 31: Menopausal symptoms for past two weeks, increasing severity, stilbestrol 1 mg. daily, orally.

	HOT FLUSHES	HEAD- ACHES	NERVOUS SYMPTOMS	BLOOD		
				HB	CELL VOLUME %	W.B.C.
July 5	+	-	+	10.7	32	8,100
July 31	++++	++++	++++	Stilbestrol 1 mg. daily		
Aug. 28	-	-	-	12.7	38	6,000
Oct. 4	-	-	-	13.0	39	10,000
Dec. 6	-	-	-	12.9	38	9,100

A résumé of the case history of a patient in whom the menopause was induced artificially at about the time of the normal climacteric. Prompt relief of all the symptoms followed the institution of therapy.

TABLE II. ARTIFICIAL MENOPAUSE, P. W. (No. 217823), AGED 21 YEARS

1938: Left cyst-oophorectomy

1939: May, right cyst-oophorectomy for huge cystadenoma

Menopausal symptoms began in June, increasing severity

Stilbestrol 1 mg. daily, orally, October 10

	HOT FLUSHES	HEADACHES	NERVOUS SYMPTOMS
Oct. 10	4	+	+++
11	8	+	++
12	5	-	++
13	4		+
14	8		
15	8		
16	5		
20	2		
24	0		

Feels fine, no symptoms, better than in years

A résumé of the treatment of an artificially induced menopause in a young woman.

Although there was an immediate response following the onset of therapy, complete relief was not obtained for a period of about ten days. Since that time she has had no menopausal complaints.

therapy is often followed by bleeding within a period of ten to twenty days. This is the characteristic withdrawal phenomenon.

Objective criteria can be used to determine the efficacy of treatment. The vaginal mucosa is an excellent indicator of estrogenic action in the human female. The author has previously called attention to changes which take place in vaginal mucosa following the cessation of ovarian activity. These changes consist of a gradual thinning of the mucosa and a change in the cellular content of the squamous epithelium. The large cells of the upper layers rich in glycogen completely disappear and are replaced by smaller inactive cells. These vaginal changes can be seen on gross examination, in small biopsies of the vaginal mucosa or in the cellular character of the vaginal smear. Papanicolaou and Shorr correlated the relief menopausal symptoms and the estrogenic changes induced in the vaginal smear (Figs. 2 and 3).

Several interesting observations were made in the therapy of these women. Many of the patients complained of breast changes following the institution of therapy. The patients developed a sense of tightness and fullness in their breasts, such as they had previously experienced in early pregnancy. They actually increased in size and became sensitive to the usual clothing. The nipples became more prominent and likewise sensitive. Some increased pigmentation of the nipples and the areolae made both of these structures more prominent. This initial breast discomfort usually disappeared on continued medication or on a reduction of the daily dose. Prolonged medication resulted in no further breast changes.

The interruption of treatment for a week or longer occasionally resulted in vaginal bleeding which persisted for several days or longer. This is the well-known estrin withdrawal phenomenon. An endometrial biopsy at this time revealed a moderate endometrial proliferation as a result of the estrogenic medication. Continued administration of stilbestrol does not result in continued proliferation of the endometrium.

Except for the fact that such bleeding after an interval of amenorrhea is disturbing to the patient, it is of no significance. Irregular periods of bleeding at the menopause always deserve the most careful scrutiny and investigation by the clinician.



Fig. 2.—The vaginal smear on a patient in the late menopause, showing the characteristic cellular content.

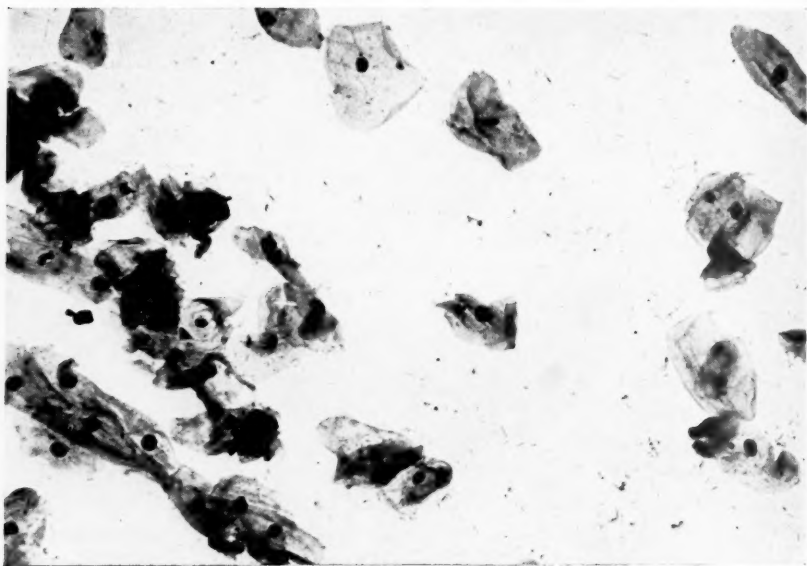


Fig. 3.—A vaginal smear on the same patient four weeks after the onset of stilbestrol therapy showing the characteristic change in the cellular content of the vagina. The large desquamated cells are rich in glycogen.

Several of the women described an increased libido after a gradual waning for a number of years. This may have been induced by the return to normalcy of the vaginal mucosa with a resultant improvement in coitus.

A careful study of the blood findings in this group of women revealed no detrimental effects as a result of the therapy. The white blood cells remained stationary in number or varied in such small ranges as to be statistically insignificant. Cytologic studies revealed no abnormal changes in the number or character of the cells. The cell volume and the hemoglobin were unchanged in most of the patients under observation. In a small group of women with marked anemias of long standing, surprising improvement occurred after short periods of stilbestrol therapy. The increase in cell volume and hemoglobin were proportionate and of such a marked degree as to be especially noteworthy (Table III). We hesitate to ascribe these changes to stilbestrol, for several factors which could influence the blood findings entered into most of these patients under observation. Nevertheless, this observation is so striking that we are giving it further study. One can at least conclude that stilbestrol in the amounts used for clinical therapy does not influence the blood constituents.

TABLE III. THE BLOOD FINDINGS IN SEVERAL PATIENTS TREATED WITH STILBESTROL, SHOWING THE MARKED RISE IN HEMOGLOBIN AND CELL VOLUME

PATHOLOGY	MENOPAUSE INDUCED	THERAPY	DATE	HB. GM.	CELL V.	W.B.C.
Croll (213970), Aged 38 Years						
Endometriosis Little bleeding	Radiation 2/26	Began stilbestrol May 22, 1 mg. daily No other therapy	2/ 1	8.3		9,000
			2/23	9.2	26%	9,400
			5/20	9.0	29%	11,000
			7/12	12.8	40%	
			10/ 2	14.0	42%	5,000
Koskonski (216213), Aged 45 Years						
Large endo- metrial polyp	Hysterectomy Bilat.salp.ooph.	Stilbestrol 6/5 5 mg. every other day	3/ 9	10.0	34%	9,300
			4/28	10.0	32%	9,850
			5/10			10,200
			6/ 3	9.1	30.5%	4,130
			8/11	13.0	42%	9,300
			9/22	13.8	43%	10,700
			10/20			10,000
			11/17			9,200
Tanneberger (206673), Aged 43 Years						
Fibroids Profuse menses Transfusions 650 c.c. 550 c.c.	Hysterectomy Bilat.salp.ooph.	Stilbestrol 4/13 5 mg. every other day	1938			
			9/29	6.6	26%	8,200
			10/20	6.2	25%	
			10/22	7.9	29%	
			10/24	8.0	23%	
			10/28	8.5	30%	
			1939			
			4/13	10.9	35%	6,300
9/ 8	13.8	40%				

PRIMARY AMENORRHEA

The onset of menstruation or puberty heralds the advent of adolescence and sexual maturity. Normal physical feminine development and the capacity for reproduction depend on normal reproductive organs which function as a result of a closely correlated endocrinal relationship. In some young women menstruation fails to take place. Although this failure is only one manifestation of an abnormal reproductive mechanism, it provides the name of primary amenorrhea.

The absence of the menses in a young woman may be the result of a lack of normal development of all or a part of the reproductive tract. The uterus may be underdeveloped, rudimentary, or its canal non-patent. The vagina may be absent or its lumen fail to provide continuity with the uterus. The gonads may be absent or abnormal. The menstrual function may be absent because of an endocrinal failure, pituitary or ovarian in origin. The anterior lobe of the pituitary provides the motor for the cyclical changes which take place in the reproductive organs. Pathologic conditions in the pituitary gland may hold these changes in abeyance or completely inhibit them. The ovaries may not be responsive to normal pituitary stimuli because of abnormal development, thereby resulting in uterine inactivity. It may be possible to determine which of these three factors operate in an individual with primary amenorrhea. It may or may not be possible to correct or remove the cause.

A lack of normal development of the sex function may have a profound effect on the physical, psychic, and even mental development of the young woman. In some of these individuals puberty and the changes it initiates are delayed into adulthood. Thus the bony skeleton may fail to develop normally as a result of delayed epiphyseal closures, secondary sex characters which differentiate the woman from the sexless child may all be absent, and the normal feminine figure fails to evolve. Associated with this lack of physical development, there usually occurs a lack of psychic development resulting in an abnormal social adjustment. The young woman may begin to brood over her physical and sexual inequalities. She magnifies their importance to such an extent that she develops an inferiority complex, a temporary or permanent psychosis, or abnormal sex relationships. Menstruation, therefore, although only one index of functioning reproductive organs, becomes of paramount importance to these individuals with primary amenorrhea.

Obviously, in the presence of only rudimentary portions of the Müllerian derivatives or in their complete absence, vaginal bleeding is impossible. When a lack of normal development of these organs is present or an abnormal endocrinal relationship interferes with normal sex activity, improvement and perhaps a restoration to the normal is, theoretically at least, possible. Every advance in endocrinology has offered one more challenge to find a solution to some of these interesting problems.

Theoretically at least, in many of the patients with primary amenorrhea, gonadotropic substances which supplant the action of the normal anterior lobe of the pituitary gland should prove efficacious. These

gonadotropes should stimulate the ovaries to normal cyclical activity so that these structures can produce the hormones necessary for endometrial growth, secretion, and menstruation. Impure gonadotropes from pregnancy urine and from gland extracts have little effect on the human ovary. Equine gonadotrope more nearly reproduces the action of the normal pituitary gland and is the most potent of our gonadotropic principles. Some results have been obtained in the treatment of primary amenorrhea, but in the majority of patients treatment with pregnant mare serum has been unsuccessful. It is possible that the ovaries of these women are primarily at fault. They may be so abnormal or undifferentiated that they are refractory to stimulation by the pituitary gland, in which event gonadotropic therapy is doomed to failure.

Estrogens must be considered as purely substitution therapy. The natural estrogens can bring about the development of the reproductive organs, the breasts, and the secondary sex characters. To accomplish this, estrogens must be administered in comparatively huge doses intramuscularly, and at frequent intervals, to maintain a constant level of blood estrogens. On the withdrawal of this hormone retrogressive changes begin, so that after a short time the structures revert to almost their previous state.

Stilbestrol has provided one ideal estrogen for the treatment of this condition. The daily oral administration of a small amount provides a sufficient estrogenic stimulus to produce physical and sexual maturity of these underdeveloped young women. The changes induced in these patients in a short period of a month or more are truly astounding. The following two case reports illustrate the profound changes that can take place on stilbestrol medication.

CASE 1.—S. B. (Unit No. 150466) was 21 years of age. When this patient was 18 years old (1936) she was admitted to our clinics never having menstruated. She has been under observation since 1934, during which time she received endocrinal substances. During 1936 and 1937 she was given various gonadotropic preparations, including, in 1938, the natural estrogens in doses from 20,000 to 100,000 units at a single administration preceding the use of mare serum hormone. No vaginal bleeding nor pronounced change in physical development occurred. Some growth of the reproductive organs appeared.

Her early history was negative. She developed a sparse growth of pubic and axillary hair at the age of 11. When 16, she became concerned over her lack of menses. She presented the typical picture of primary amenorrhea, was typically feminine in type, but retained the prepubertal characteristics, square shoulders, narrow box-like hips, and android pelvis. Her appearance was juvenile. X-rays revealed normal epiphyseal growth with retardation of closures in the proximal phalanges. The sella turcica was normal. The visual fields were normal. The basal metabolic rate varied from -9 to -17. The breasts were hardly visible and could not be demarcated except for rudimentary nipples. The flattened pale pink areolae measured 8 mm. in diameter. Pubic hair was sparse and silky. The labia majora were flat and hardly evident; the labia minora were thin and almost transparent. The vagina was narrow, admitting the finger with difficulty, and there were no palpable rugae. The uterus was infantile in type, with a large cervix and a small corpus.

She was placed on stilbestrol on May 1 and has continued taking 1 mg. daily by mouth, with but few periods of rest. She tolerated the drug well. She had a

moderate anemia at the onset of therapy, 8.8 Gm. Hb., cell volume 25 per cent, which has corrected itself so that at present the Hb. is 13.8 and cell volume 41 per cent. Monthly studies revealed little fluctuation in white blood count, averaging approximately 8,000. Other laboratory examinations have been negative.

Marked physical changes have taken place as demonstrated by the illustrations (Figs. 4 and 5), the most gratifying to the patient being the occurrence of bleeding. A pinkish discharge occurred May 22, 23, and 24 and periods have occurred during June, August, September, and November. Most of these periods occurred even with continued use of stilbestrol, although the September period was provoked by withdrawal of the drug for two weeks. The flow has been moderate lasting from three to five days. Biopsies revealed a moderate proliferative phase of the endometrium.

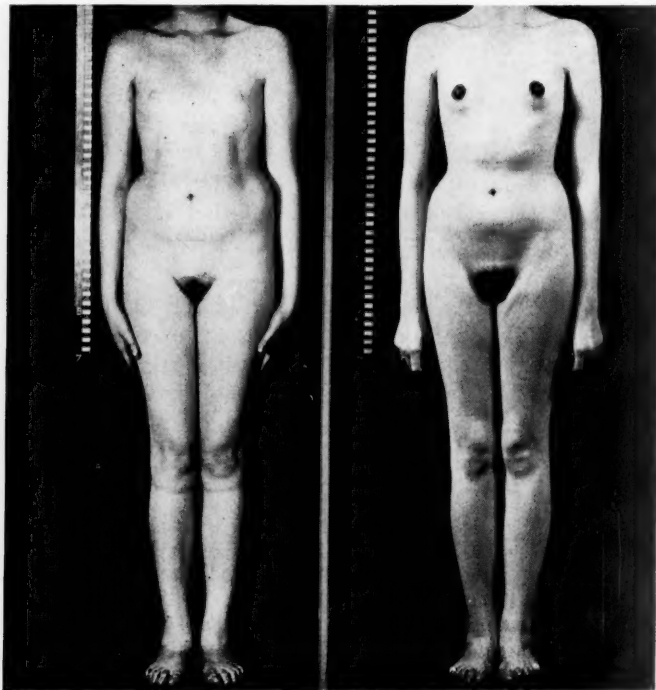


Fig. 4.

Fig. 5.

Fig. 4.—S. B. (Unit No. 150466). Before the onset of stilbestrol therapy. Note the lack of breast development, the small pale nonpigmented nipples and areolae, the scant growth of pubic hair, and the general juvenile appearance.

Fig. 5.—S. B. (Unit No. 150466). The young woman has been on 1.0 mg. stilbestrol daily for four months. Note the breast development as well as the nipple growth and the marked pigmentation of the nipples and areolae. There is likewise an increased pigmentation of the linea abdominalis. A thick growth of pubic hair has occurred. There has been a marked change in the general physical appearance of the patient.

The patient developed the typical mature feminine figure, the angular appearance disappeared and a luxuriant growth of hair over the pubis and under the axillae appeared. The breasts have enlarged and the nipples have increased in size, with pigmentation of the areolae and nipples. Pigmentation is also present in the linea of the abdomen and other areas. The external genitalia have reached the stage of normal adult sex development. The vagina has increased in roominess and length, with prominent rugae. Biopsy reveals many layers of cells in the squamous epithelium. The uterus has increased to approximately normal size, with a normal ma-

ture ratio between the corpus and cervix. Psychic changes have been phenomenal. The patient had been morose, unhappy, and a defeatist, but after treatment began a marked change took place in these respects. With a renewed interest in life her whole demeanor has changed, and she is now a normal healthy young woman who works hard and enjoys social relaxations.

CASE 2.—R. F. (Unit No. 219149), aged 25 years, was admitted to our clinics early in 1939 for primary amenorrhea. She had been treated elsewhere for two years. Thyroid, estrogenic hormones, and anterior pituitarylike substance had proved ineffective.

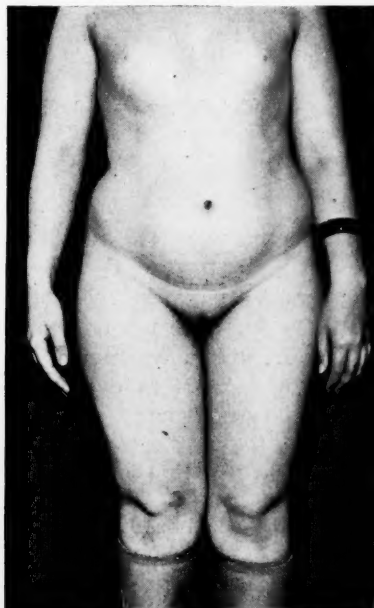


Fig. 6.

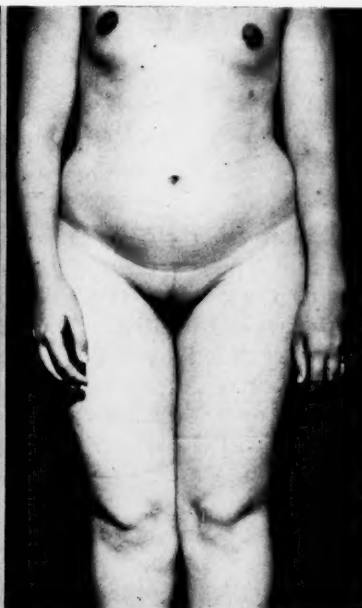


Fig. 7.

Fig. 6.—R. F. (Unit No. 219149). Before the onset of stilbestrol therapy. The lack of breast development and the scant growth of pubic hair is particularly well shown in this photograph.

Fig. 7.—R. F. (Unit No. 219149). This young woman has been on 1.0 mg. stilbestrol daily for three months. There has been a marked enlargement of the breasts including marked growth of the nipples. The pigmentation of the nipples and the areolae is particularly striking. Note likewise the increased pigmentation of many small localized areas which were hardly evident prior to therapy. The increased pigmentation of the *linæ abdominalis* is likewise striking. There has been a marked growth of pubic hair.

Her early history was negative, except that she was a premature baby. Growth ceased at 15 or 16 years of age. Her appearance was typically feminine, but she had retained juvenile characteristics. X-rays revealed well-advanced epiphyseal closures. The sella turcica was small. A constriction of the visual field was present, but there were evidences of a pathologic pituitary gland. Basal metabolic rate was -7 . The breasts were neither visible nor palpable. The nipples were tiny and the areolae small. The pubic and axillary hair was scant. The external genitalia were underdeveloped. The labia majora were flattened and the labia minora thin and of tissue paper consistency. The vagina admitted one finger with difficulty, the vaginal walls were smooth and shiny. The uterus was smaller than normal, consisting predominantly of cervix.

She was placed on 2 mg. of stilbestrol daily, orally in June, but this amount was reduced in several weeks to 1 mg. She tolerated it well at first, but later complained

of occasional nausea on arising. Blood examinations varied little during therapy. Hemoglobin averaged from 13 to 14 Gm., cell volume 37 to 42 per cent and white blood cells about 6,000. (Figs. 6 and 7.)

She improved markedly during a four months' period. Her first flow occurred July 1, lasting two days. She bled for eight days in August, two in September, and five in October. These periods occurred in spite of continuous therapy. Four biopsies were obtained on the first day of each flow with little endometrial variation from moderate proliferation. Prior to therapy no endometrium could be obtained. The external genitalia assumed the normal adult type. The vagina increased in diameter, and the vaginal mucosa assumed the normal adult type. A faint bluish discoloration is evident in the mucous membranes of the vagina and cervix. The corpus grew in size and length. Pubic and axillary hair grew markedly. The breasts increased in size and now stand out prominently from the chest wall. The nipples increased in size and prominence with marked pigmentation. Small areas of pigmentation on the body are more pronounced.

The patient has improved mentally, becoming cheerful, happy, and feeling as if she is a normal individual. This psychologic change is most important to the well-being of this individual.

DISCUSSION

Many interesting observations have been made in the treatment of this group of patients. Stilbestrol completely replaces the estrogenic activity of the ovary. It produces sexual maturity in the immature female with the exception of ovarian function. The prepubertal state is rapidly replaced by the physical and organic development of the mature woman. All of the secondary sex characters develop. The reproductive organs assume the normal adult type. The undifferentiated juvenile physical characteristics give way to the mature feminine form. The speed of the transition is remarkable, for all this is accomplished in a period of several months, whereas normal adolescence requires three or four years. The gonads are the only reproductive organs that are not affected and remain dormant.

It was possible to produce some of these changes by means of the natural estrogens when they were administered at frequent intervals and in large doses. It has not been possible to produce the degree of physical and sex development seen in this group of women. Furthermore, it has been impossible to maintain the development for long periods of time so that the patient would be benefited by the change. The natural estrogens were administered intramuscularly at varying intervals and for short periods of time. This mode of medication probably resulted in varying concentrations of blood estrogens not conducive to optimum results. Oral medication can be easily maintained over long periods of time, thereby producing a constant estrogen level in the blood and tissues.

Obviously, this substitution therapy must continue in order that these young women remain normal. When natural estrogens only were available, continued therapy was impossible and undesirable. Now that it is possible to take a small tablet once a day or less often, prolonged substitution becomes entirely feasible. There can be no question as to the desirability of continued therapy in these young women, providing this therapy is safe and no injurious effects occur. Only careful clinical observations and experimental studies over long periods of time will answer these questions. No one doubts the wisdom of continued sub-

stitution therapy in hypothyroidism, in diabetes, and in other glandular deficiencies. Why should one doubt the wisdom of continued therapy in hypo-ovarianism?

The amount of stilbestrol necessary to maintain the optimum development of the individual is difficult to ascertain. Larger amounts of the drug are necessary during the transitional period, but small amounts may suffice to retain the desired changes. About 1 mg. daily has been sufficient to prevent any regression, and it is entirely possible that this amount is too large. Careful endocrinal assays may reveal the optimum daily consumption of this drug. Nature is very lavish in the production of its own endocrines, and much of the excess is destroyed or eliminated. Substitution therapy need not be that extravagant.

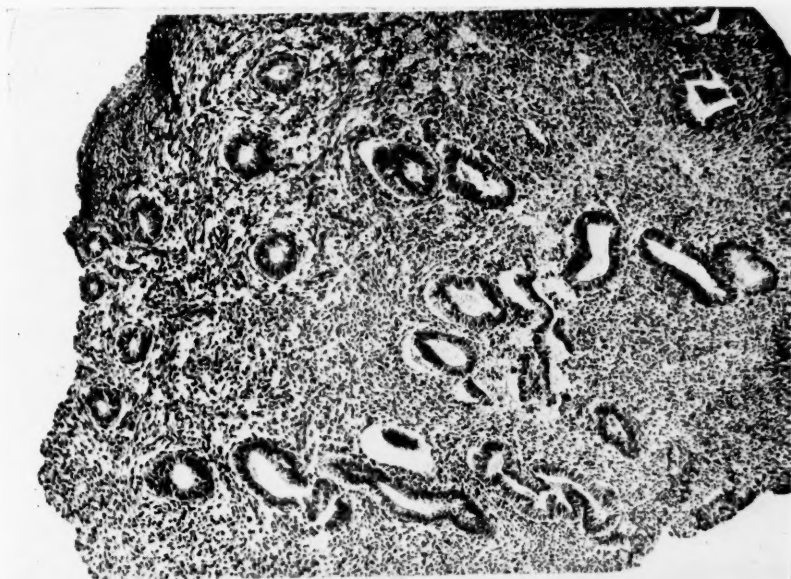


Fig. 8.—A biopsy of the endometrium obtained on August 15, the first day of an anovulatory menstrual flow which lasted eight days. A moderate proliferation of the endometrium is present which is representative of the endometrial picture of this group of women with primary amenorrhea who are under treatment with stilbestrol.

Periods of bleeding occur seven to twenty days following the sudden withdrawal of the drug as well as on continued medication. These periodic bleedings occur with some degree of regularity. The only difference between true ovulatory menstruation and these anovulatory bleedings is in the endometrial picture. The mucosa of the uterus develops a moderate proliferative phase (Fig. 8). Continued medication with stilbestrol does not result in continued proliferation of the endometrium. The endometrial picture resembles that normally encountered prior to ovulation. The bleeding is preceded by the usual premenstrual prodromas, and subjectively these periods are very much like normal menses. The blood loss is scant in amount and there is no loss of

desquamated endometrial fragments. The character of these periodic bleedings provides additional evidence as to the fundamental physiologic mechanism underlying normal menstruation.

The development of the breasts is limited to a growth of the duct system. No changes take place in the secretory acini, for these are not stimulated by the estrogens. The nipple and the areolae show pronounced growth changes. No secretion is present in these breasts.

The pigmentation that occurs is most marked in the nipples and the areolae, but the linea alba as well as other mildly pigmented areas become intensely discolored. As the treatment is continued, these pigmented areas increase in intensity. This unusual pigment response is much greater in degree than that usually seen in normal pregnancy. The natural estrogens provoke pigmentation, but not in the degree seen in these patients. We are conducting studies into the nature of this pigmentation.

CONCLUSIONS

Stilbestrol, a new synthetic estrogen unrelated to the natural estrogens, has tremendous clinical possibilities. The oral administration of the drug can reproduce all the changes induced by the natural estrogens much more effectively and to a greater degree. It replaces the estrogenic action of the ovary. Many clinical conditions which are the result of a deficient ovarian activity or its complete cessation can now be easily and successfully treated. The treatment of the menopause and primary amenorrhea with stilbestrol is discussed in this paper. Other conditions under treatment at the present time will be discussed at a later date.

The widespread clinical use of stilbestrol must await more adequate evidence as to its possible toxicity. Pharmacologic experiments involving the long-continued administration of moderate amounts of this drug must be carried out to determine late undesirable effects. Careful clinical observations must be continued with the most guarded approach until such time as the lack of toxicity of the drug can be firmly established.

The author wishes to express his thanks to Dr. Anderson and Dr. Morrell of E. R. Squibb and Sons and to the Winthrop Chemical Company for their generous supplies of stilbestrol.

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DISCUSSION

DR. FRED L. ADAIR.—I do not believe we should accept this very potent agent for general clinical use until we know more about its benefits and more about its abuses. We find doses of $\frac{1}{2}$ mg. or 1 mg. highly effective in controlling menopausal

symptoms but we must not necessarily assume that that is the proper dose for a woman with amenorrhea or for a woman in whom suppression of lactation is desired.

I wish to call attention to two observations made by Dr. Davis. The first is the effect it has on the pigmented cells. There is nothing known regarding what effect stilbestrol will have on such cells and we should be very careful with its administration in a patient with pigmented moles because little is known about its stimulating effect. The second is the stimulation of the hematopoietic cells with increased hemoglobin. It would seem with this observation that if the drug is irritating to these cells there might be some stimulation and an overdosage would be harmful. Studies are being carried out in regard to the effects of the administration of the drug on the liver and hematopoietic system. We are attempting to study this drug by very carefully controlled experiments.

DR. PHILIP F. SCHNEIDER.—The question of the toxicity of stilbestrol is of importance from the standpoint of safety as well as economy. The criticism of toxicity as manifested by nausea and more recently the claim of retention of bilirubin have been presented. Sevringhaus, Davis and others have discounted this criticism by the observation that nausea has disappeared by reduction of dosage. This would suggest the possibility that clinical evidence of toxicity as well as experimental evidence of retention of bilirubin may be due to excessive dosage rather than to inherent toxicity of the preparation.

Control of estrogenic therapy by means of vaginal smears, using the technique of Papanicolaou in menstrual, reproductive as well as menopausal conditions in our experience would seem to substantiate the above conclusions.

Until the factor of toxicity is more definitely repudiated by more additional evidence it seems obvious that this particular synthetic estrogenic preparation should be used with extreme caution.

DR. DAVIS (closing).—The most important problem presented is the possible toxicity of this new drug. We have treated almost 200 patients for varying lengths of time, many for almost a year. The absence of all symptoms or signs indicative of toxicity, the absence of skin rashes and of neurological symptoms were, indeed, surprising, in view of some of the published reports. The outstanding thing in the therapy of these patients was the absence of all undesirable reactions.

Few patients complain of nausea when the daily dose of the drug is 1 mg. or less. In a number of instances the nausea which was present during the first few days of the administration disappeared on the continued use of the therapy. The usual estrin withdrawal bleeding can be readily induced by stilbestrol medication. However, in some of the patients under continued therapy, periods of bleeding occurred in spite of the constant estrin level. The endometrial changes were the same in both instances.

Obviously, in the treatment of primary amenorrhea the use of an estrogenic substance is entirely substitution therapy. In order to maintain the desirable changes induced by continued administration of this preparation, these young women would have to take the drug until they are 40 or 45 years old. If this drug is found to be nontoxic, this is not objectionable. In all endocrine deficiencies, only substitution therapy is available. Hypothyroidism has to be treated indefinitely. There is no reason to feel that one can cure hypogonadism by means of estrogenic medication. Continued medication would be desirable for these girls benefit tremendously by such therapy. Their entire outlook on life becomes changed. Their work improves and they gain renewed interest in living.

HYPERTHYROIDISM AND PREGNANCY*

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AS HYPERTHYROIDISM is a rare complication of pregnancy, the experience of most obstetricians is limited to a few cases. It is perhaps for this reason that one finds in the literature such marked disagreement as to treatment, as is evidenced by the varied opinions relative to the use of iodine, surgery of the thyroid gland during pregnancy, continuation of the pregnancy, and therapeutic abortion.

In the Woman's Clinic of the New York Hospital in the past seven years, 18 cases of hyperthyroidism complicated by pregnancy were noted in 23,439 patients, an incidence of only 0.076 per cent. Clinically these cases were divided into diffuse exophthalmic goiter (12 cases), adenomatous goiter (4 cases), and hyperthyroidism without excessive goiter (2 cases). The symptoms of hyperthyroidism were the same as for nonpregnant women, and need not be given here. The symptoms antedated pregnancy in 10 cases, while 8 patients developed symptoms during the pregnancy, and in the latter group were 3 private patients in whom the symptoms were thought to have been precipitated by the knowledge of pregnancy. Only 1 patient could date symptoms to a previous pregnancy, and another patient had been subjected to two thyroid operations without relief. The thyrotoxicosis was regarded as severe in 5 cases (3 having a nodular goiter), moderately severe in 9 cases, and mild in 4 cases. The average duration of symptoms was 3.2 years before the current pregnancy.

TABLE I. THE AVERAGE DURATION OF PREGNANCY IN 18 CASES OF HYPERTHYROIDISM

	NUMBER OF CASES
40 weeks	10
37 weeks	3
Abortions	5
Total	18

The average duration of pregnancy in the 18 patients is shown in Table I. Of the 5 abortions, 4 were performed for therapeutic reasons, 22.2 per cent, while one occurred spontaneously. The majority were delivered at term.

The average age was 31.6 years, which is nearly eight years older than the average for the clinic population. There were 12 multiparas and 6 primiparas, with an average number of 2.6 pregnancies (including abortions) for each patient. Hinton gives a higher incidence in primiparas, while Portis and Roth found a higher incidence in multiparas.

*Read at the Section of Obstetrics and Gynecology, New York Academy of Medicine, December 26, 1939; and read in part at the Graduate Fortnight of the Academy at the New York Hospital on October 26, 1939.

Cardiac disease on a valvular basis, irrespective of the thyroid disease, was present in 2 cases. The average pulse rate during the ante-partum course was 104 per minute, and after iodine therapy had been given for about ten days, there was a slight decrease in the rate to 96 per minute.

The average weight at the beginning of pregnancy was 58 kilograms (127.6 pounds), which is approximately the same as the average for the clinic according to Pastore. The average weight gain during pregnancy was 14 kilograms (30.8 pounds), or 24 per cent; which is the same as the clinic figure. However when the 13 cases reaching viability or term are studied, it is observed that 6 patients, or 46.1 per cent, failed to gain weight properly; in fact, two patients lost weight. This failure to gain weight in a normal manner was attributed to the hyperthyroidism.

Toxemia of pregnancy was observed in 10 cases, or 76.9 per cent of the cases reaching viability or term; the clinic incidence of toxemia is 6.7 per cent. The classification of the American Committee on Maternal Health was used, and the types of toxemia are given in Table II.

TABLE II. THE TYPES OF TOXEMIA OF PREGNANCY IN HYPERTHYROIDISM

	NUMBER OF CASES
Pre-eclampsia, severe	2
Pre-eclampsia, mild	2
Hypertensive disease	2
Renal disease	4
Total	10

From the average basal metabolic rate as shown in Fig. 1, it will be seen that for the first, second, and third trimesters of pregnancy, the values are plus 26 per cent, plus 36 per cent, and plus 35 per cent, respectively. There was a moderate reduction in the rate to plus 26 per cent following iodine therapy. A probable basal metabolic rate curve for normal pregnancy is also shown in Fig. 1, and was obtained as shown in Fig. 3. This curve shows a normal rise in the metabolic rate to plus 12 to 16 per cent at term. On this basis one could expect a rise in the hyperthyroid patients to plus 45 per cent, but this did not take place. This suggests that the thyrotoxicosis may even be ameliorated by the pregnancy. On the tenth to twelfth post-partum day, the rate is still elevated as before delivery, whereas in normal patients a return to normal readings is observed. Since delivery has removed the products of conception, and consequently the active protoplasmic mass of the fetus, the elevated rate post-partum is evidently due to thyroid hyperplasia. Is it not hyperplasia of the thyroid gland concomitant with pregnancy, rather than protoplasmic mass, that causes the increased metabolic rate in normal patients?

TABLE III. THE TYPES OF DELIVERY OR TERMINATION OF PREGNANCY

	NUMBER OF CASES
Spontaneous	10
Operative	3
Abortion	1
{ Spontaneous	1
{ Induced	4
Total	18

The type of delivery is shown in Table III and one sees that 10 cases, or 76.9 per cent, had a spontaneous delivery. Of the operative cases, cesarean section was performed for placenta previa, low forceps were applied for fetal distress, and a Voorhees' bag was inserted to initiate labor because of toxemia. The average duration of labor was sixteen hours.

TABLE IV. THE TYPES OF ANESTHESIA USED FOR DELIVERY OR TERMINATION OF THE PREGNANCY

	NUMBER OF CASES
Nitrous oxide, oxygen, ether	12
Cyclopropane	2
Local infiltration	2
Avertin	1
No anesthesia	1
Total	18

The types of anesthesia used for delivery or for the termination of pregnancy are given in Table IV. Nitrous oxide, oxygen, and ether mixture was administered to two-thirds of the patients. Since the duration of the anesthesia was short (the majority of the patients being multiparas) ill effects from the nitrous oxide were not anticipated. Morphine and scopolamine, or rectal ether analgesia, was used during labor in only 6 patients.

The average weight of the infants was 3,495 Gm. (7 pounds, 11 ounces), which agrees with the average weight of infants in the clinic. There was no fetal mortality in babies weighing 1,500 Gm. and over.

The puerperium was mildly febrile in 2 cases. There was a questionable thyroid crisis immediately after delivery in 1 case. Lactation occurred normally in 7 patients and was permitted in these. There was no maternal mortality.

TREATMENT

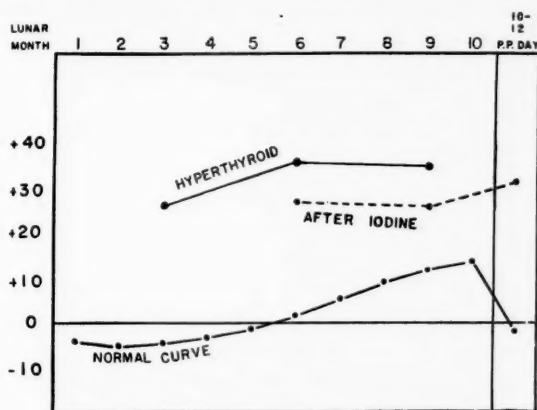
Iodine in the form of Lugol's solution or syrup of hydriotic acid was used in all but 4 of the cases in which therapeutic abortion was performed. An appreciable lowering of the basal metabolic rate was observed following iodine therapy, as shown in Fig. 1. A similar decrease has been observed by Mussey, Plummer, and Boothby.

Dietary advice was given, and rest during the day was insisted upon. Psychotherapy was administered, and Social Service assistance was utilized to improve the home environment and minimize stress and strain. Hospitalization on one or more occasions during the ante-partum course was considered necessary in 11 of the 13 cases reaching viability or term. The average duration of such an admission was nineteen days. These patients were also admitted for an average of ten days before their confinement.

Adequate ante-partum care played an important part in carrying these patients to term, since the weight, pulse rate, blood pressure, and the basal metabolic rate could be observed at regular intervals. Close cooperation with the medical and surgical services was considered important in the care of the patients.

Thyroidectomy was not performed during pregnancy, even though 4 patients had an adenomatous type of goiter, although operation was advised but refused in one such case. However in the first post-partum year, operation was advised in all of the 5 severe cases, and was permitted in 3 of the patients.

Therapeutic abortion was performed in 4 patients, or 22.2 per cent, which is a high incidence. However 3 of these were private patients.



BASAL METABOLIC RATE IN PREGNANCY
WITH HYPERTHYROIDISM - 18. CASES

Fig. 1.

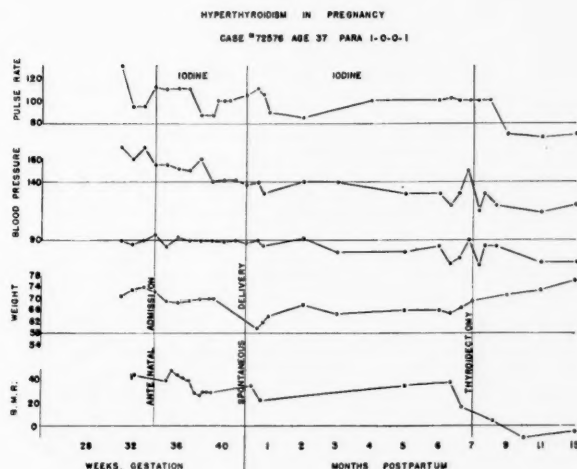


Fig. 2.

CASE REPORT

This case illustrates the clinical management and treatment of a patient with hyperthyroidism and pregnancy. The patient was a 37-year-old woman, white, para 1-0-0-1, with a normal past obstetric history. The thyroid symptoms antedated the present pregnancy by only several months. She registered in the clinic in the thirty-second week of gestation, at which time the pulse rate was elevated to 100 per

minute, the blood pressure was 170 systolic and 90 diastolic (millimeters of mercury), and there was no albumin in the urine. There was a palpable adenomatous goiter, and the basal metabolic rate was plus 45 per cent. A clinical diagnosis of adenomatous goiter, and toxemia of pregnancy was made and the patient was admitted to the hospital where she remained until delivery.

Observations of the pulse rate, weight, blood pressure, and the basal metabolic rate were made as shown in Fig. 2. Syrup of hydriotic acid was given, the patient was confined to her bed, and a routine low protein diet was ordered because of the toxemia of pregnancy. This diet has 275 Gm. of carbohydrate, and was changed to a high carbohydrate diet when the hyperthyroidism became more evident. There was gradual improvement, the weight increased slightly, and the blood pressure became lower, and the basal metabolic rate decreased to plus 29 per cent. The fluid intake averaged 2,500 c.c. daily, with a urinary output of 1,200 to 1,500 c.c. daily. The fundi oculi showed suggestive signs of early sclerosis. The blood chemical studies before delivery have been summarized in Table V. The values are essentially normal except for the lowered carbon-dioxide combining power.

TABLE V. THE AVERAGE BLOOD CHEMICAL VALUES (AVERAGE OF 2 TESTS) IN THE CASE REPORTED

Nonprotein nitrogen	34.7 mg.
Uric acid	3.1 mg.
Chlorides	493.0 mg.
Sugar	88.0 mg.
Carbon dioxide	39.6 volumes per cent
Urea clearance	157.0% in 2 hours
Phenolsulphonephthalein	96.0% in 2 hours

After a stay of forty-two days in the hospital, and since the baby was viable, and because the uterus had become irritable, a medical induction of labor consisting of castor oil, quinine, an enema, and eight doses of pituitrin intranasally, was given. It was successful, and after a short labor of ten hours, delivery was accomplished spontaneously. No analgesia was used, and nitrous oxide and oxygen was given for several minutes for the actual delivery. The infant weighed 2,900 Gm. (6 pounds, 7 ounces), and was in good condition. There was no thyroid crisis.

On the tenth postpartum day the basal metabolic rate was plus 21 per cent, and six months later it was plus 34 per cent. Thyroidectomy was performed in the eighth month post partum. Prior to the operation, as shown in Fig. 2, the patient failed to gain weight, and the blood pressure was still elevated, although the blood pressure was nearer normal. After the operation immediate improvement was observed, the patient gained weight, the pulse rate became normal as did the basal metabolic rate and blood pressure.

DISCUSSION

The data presented above are from a study of only 18 cases, nevertheless a period of seven years is covered, during which time 23,439 patients were delivered. These cases illustrate the policy of the Woman's Clinic with regard to hyperthyroidism and pregnancy. The incidence of this complication of pregnancy was only 0.076 per cent, which is in agreement with the incidence of Wallace in Brooklyn, as shown in

TABLE VI. THE INCIDENCE OF HYPERTHYROIDISM AND PREGNANCY

			INCIDENCE
Javert	New York	18 cases in 23,439	0.076%
Wallace	Brooklyn	9 cases in 11,571	0.077%
Portis and Roth	Chicago	14 cases in 1,000	1.4%
Yoakum	Detroit	(Quoted by Wallace)	3.7%
Markoe	New York	8 cases in 100,000	0.008%

Table VI. This table also shows a higher incidence in the cities in the goiter district. The very low incidence of Markoe was recorded in the days before the basal metabolism test was in general use.

Iodine was used without hesitation for long periods of time even in the patients with nodular goiter without evidence of harmful effect. Davis has had similar experience and began the use of iodine in pregnancy in 1926, following Marine and Kimball's reports (1921) on the prophylactic use of iodine in adolescent goiter. Mussey cautions against the use of iodine in adenomatous goiter, but advises it in diffuse exophthalmic goiter. Graham has shown iodine to be beneficial in both types of hyperthyroidism.

The benefits of iodine extend also to the fetus. Else and Davis state that congenital goiter may develop unless iodine is administered. Debrececa states that iodine is compulsory during pregnancy in Berne, Switzerland. Fenger has found iodine in the thyroid gland in the fetal calf as early as the third month of pregnancy.

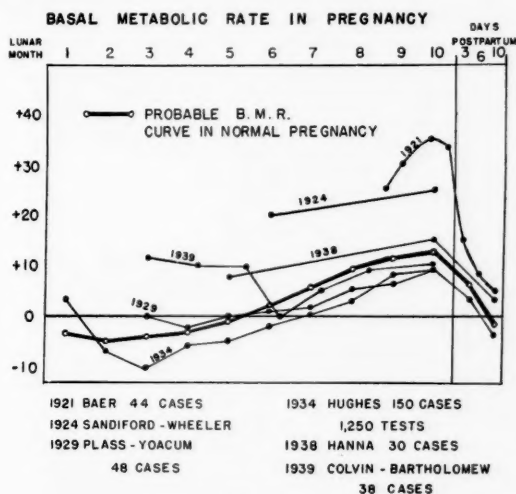


Fig. 3.

The incidence of toxemia of pregnancy was 76.9 per cent, which is a marked increase over the clinic figure of only 6.7 per cent. Are we to again give credence to the older views that toxemia and thyrotoxicosis are related to each other? Colvin and Bartholomew found an incidence of toxemia of pregnancy in 38 per cent of patients having an elevated basal metabolic rate. Conversely, Stander and Peckham, in an earlier study, showed an increased metabolic rate in patients with toxemia. Wiegand has shown an increased function of the thyroid gland in eclampsia, while Anselmino and Hoffmann, Soule, and others have demonstrated an increased amount of a thyroxinlike substance in pregnancy.

The basal metabolic rate in pregnancy was first studied by Magnus Levy in 1887, and since then by many other investigators, including Baer, Sandiford and Wheeler, Hughes, Plass and Yoakam, Hanna, Colvin and Bartholomew. The data obtained by these workers are shown in Fig. 3, and the earlier tests show values up to plus 25 to 35

per cent for the last trimester of pregnancy. A probable basal metabolic curve for normal pregnancy is also shown in Fig. 3, based on the data of the investigators named, as well as from current knowledge of the test; and it is generally believed that an increase to plus 12 to 16 per cent occurs at term. The lower rate is probably due to better apparatus and technical skill, as well as the education of the patients after several tests. DuBois states that the present normal standard, which is now arbitrarily placed at zero, is probably nearer minus 5 per cent for a patient having had several tests (as in the several trimesters of pregnancy).

The increase in the metabolic rate during gestation has been attributed by Sandiford and Wheeler, Hanna, and others to active protoplasmic mass of the fetus. Hanna adds that thyroid hyperplasia associated with pregnancy may also be a factor, which is tenable since visible hypertrophy of the gland occurs in 41 per cent of pregnant women according to Davis, and palpable enlargement up to 90 per cent according to Hinton. In the hyperthyroid patients in this report, the

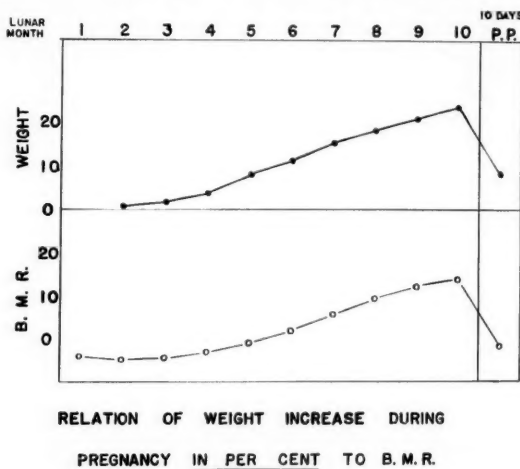


Fig. 4.

metabolic rate remained elevated after delivery had removed the products of conception, which may be interpreted as indicating that thyroid hyperplasia and not active protoplasmic mass affects the basal metabolic rate. It is to be remembered that part of the weight gain in pregnancy is due to hydremia and amniotic fluid.

The monthly average weight gain in pregnancy has been studied in 2,500 normal patients by Pastore. If the increase is expressed in percentage, a curve is obtained as shown in Fig. 4, an increase to 24 per cent occurring at term. In comparing this weight curve with the probable basal metabolic rate curve, it is evident that they parallel each other, with a decrease in both after delivery. This supports the theory of active protoplasmic mass as the cause of the normal increase in the basal metabolic rate in pregnancy. However as pointed out above, thyroid enlargement occurs in 40 to 90 per cent of the patients in preg-

nancy, and Abbott has demonstrated hyperplasia in the thyroid glands of pregnant cows on histologic examination. One may conclude that the normal rise in the basal metabolic rate is due to thyroid hyperplasia concomitant with pregnancy. In the hyperthyroid patients of this study, the rate was essentially the same in the second and third trimesters of pregnancy (plus 36 per cent and plus 35 per cent) as it was post partum (plus 33 per cent), showing that hyperactivity of the thyroid gland and not the protoplasmic mass of pregnancy was responsible. On the other hand, it may be said that this shows aggravation of the hyperthyroidism by the pregnancy, which was not substantiated by the clinical course of the patients. In fact, the failure of the metabolic rate in the third trimester to exceed that of the second trimester indicates that pregnancy was exerting a beneficial effect. Portis and Roth state that in certain cases the thyroid condition may even be ameliorated, which view is supported by the investigations of Bodansky and Duff on rats. They showed that pregnant rats tolerated larger doses of thyroid extract than did the nonpregnant animals.

Therapeutic abortion was performed in 22.2 per cent of the patients, which seems high, but 3 of these were private patients. If we study the 171 abortions done for therapeutic reasons in the Woman's Clinic in the past seven years, it is learned that 4 or 2.34 per cent were performed because of hyperthyroidism. Wallace and Bothe state that it is never indicated, and Means says that the thyrotoxicosis and not the pregnancy should be interrupted. Hinton makes an exception if cardiac changes are marked, or if the hyperthyroidism is of the fulminating type. Fahrni states that interruption is more dangerous than a well-performed thyroidectomy, especially in the third to the fifth month of gestation. It is to be remembered that abortion does not cure the thyroid disease, and carries an added risk of infection, and even of a thyroid crisis.

Thyroidectomy was not performed in the author's cases, although it was advised in 1 case. This operation during pregnancy has its advocates in Mussey, Polowe, Portis and Roth, Means, Frazier, Fahrni and others. Mussey favors operation in adenomatous goiter in preference to iodine therapy. On the other hand, Brams says that 90 per cent of pregnant women can be carried to term without thyroidectomy, and Bothe agrees that it is rarely necessary. Thyroidectomy during pregnancy is objectionable on the grounds that the gland has become hyperplastic and vascular, making it difficult to judge how much of the gland to remove. A second operation may be necessary, or myxedema may develop. Furthermore the effects of the operation on the unborn child are uncertain. In normal pregnant dogs, according to Stander, thyroidectomy results in large thyroid glands in the puppies. Williamson has cautioned the profession regarding this possibility in human beings, and advises thyroid extract, iodine, sedation, and rest if a thyroidectomized woman becomes pregnant. This advice probably also applies to those operated upon during pregnancy.

Hospitalization during the ante-partum course was considered important in the majority of patients carried to term. Many of the pa-

tients were admitted to the hospital more than once for an average stay of nineteen days. These patients were likewise admitted for ten days before delivery.

Analgesia during labor should have been used more frequently. The use of nitrous oxide anesthesia is also open to criticism, not only because of the hyperthyroidism, but also because of the associated toxemia of pregnancy. Lahey advises cyclopropane for operation in these patients, since their oxygen requirement is 2 to 3 times greater than in normal patients. However no ill effects were observed following nitrous oxide, oxygen and ether inhalation, probably because the duration of the anesthetic was short, since most of the patients were multiparas. Local anesthesia for the episiotomy, preceded by adequate analgesia, should be very satisfactory. It is being used more and more in patients with toxemia, diabetes, tuberculosis, and cardiac disease.

The association of hyperthyroidism and sterility has been repeatedly mentioned in the literature, including the recent review of the thyroid gland and pregnancy by Mussey. He quotes Carey, Randall, Titus, Bloss, and others, as giving thyroid extract to sterility patients to improve their fertility. If the presumption is correct, hyperthyroid patients should be unusually fertile, which is certainly not the case. Mussey reports only 42 pregnancies in 7,228 patients with hyperthyroidism, an incidence of 0.6 per cent. Conversely, hyperthyroidism and pregnancy has a lower incidence of 0.07 per cent in the author's series. Since this study was made, subsequent pregnancy has been reported in only 1 case, and only one patient could date the onset of hyperthyroid symptoms to a previous pregnancy. However the role of contraception in these patients must be considered as a possible reason for their sterility.

Follow-up studies for a year or more in the majority of the cases revealed no evidence of aggravation of the hyperthyroidism by the pregnancy in the mild or moderately severe cases. This was also true of the 5 severe cases, three were operated upon in the first post-partum year, although one of the severe cases was regarded as slightly worse because of the pregnancy.

SUMMARY AND CONCLUSIONS

1. There were 18 cases of hyperthyroidism in 23,439 pregnant women, an incidence of only 0.076 per cent, which is a low figure in a seacoast city as compared with higher incidences in cities in the goiter district.

2. With proper treatment, patients suffering from hyperthyroidism may safely go through a pregnancy, and sometimes even be benefited thereby. Hospitalization for evaluation and stabilization may be necessary several times during the ante-partum course.

3. Iodine therapy in our experience is without danger even over long periods of time both during and after pregnancy. There is some question regarding ill effects of iodine in adenomatous goiter, while its use in diffuse goiter is generally accepted.

4. Therapeutic abortion is rarely indicated, although it was performed in 22 per cent of the cases, most of which were private patients.

5. Thyroidectomy was not performed during pregnancy. The optimum time for this operation is believed to be in the first post-partum year in the cases where it is indicated, so that the effects of pregnancy on the gland are no longer present. However thyroidectomy may be performed regardless of the pregnancy in the individual case, as shown by reports in the literature.

6. The high incidence of toxemia of pregnancy (76 per cent) in the present study seems to be of significance, and raises the question of a common factor in toxemia and thyrotoxicosis.

7. The increase in the basal metabolic rate in normal pregnancy may be entirely due to thyroid hyperplasia concomitant with the pregnancy, rather than to the active protoplasmic mass of the fetus. In the 18 cases, the rate was virtually the same in the second and third trimesters of pregnancy, and immediately post partum when the products of conception had been delivered; normally the basal metabolic rate returns to nonpregnant levels.

8. A probable basal metabolic rate curve for normal pregnancy, based on the current knowledge of the test, is presented.

9. Pregnancy may have an ameliorating effect on the hyperthyroidism. Only one case was thought to have been aggravated by the gestation.

10. Nitrous oxide, oxygen, and ether anesthesia was used for delivery which was usually spontaneous and of short duration, since most of the patients were multiparas. Local anesthesia is preferred.

11. A case report showing the management and clinical course as practiced in the Woman's Clinic of the New York Hospital is presented.

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ENDOMETRIOSIS*

A STUDY OF 260 PRIVATE HOSPITAL CASES

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TOO often perhaps, reports are made concerning the diagnosis and treatment of various conditions based upon the records of large clinics, which are administered by experts. These results should be much better than the average. One wonders if a cross section of the care of these conditions by the average surgeon, working in an average private hospital, might not be very instructive, and although perhaps renewing our humility to some degree by the less excellent mortality and morbidity records, give a more exact estimate of the treatment accorded patients of the higher social levels.

The subject of endometriosis is excellently adapted to a review of the records of private hospitals, because it has been the observation of numerous investigators that this condition is more prevalent among women in the middle or upper strata of society.

In reviewing the voluminous literature on endometriosis one is impressed not only by the large percentage of failures to make a pre-operative diagnosis, but by the lack of standardization in the treatment of this condition. Also in discussing the problem with our colleagues, particularly general practitioners and general surgeons, the conclusion is forced upon us that there is too often a failure to make a diagnosis with the abdomen open, and consequently a failure to apply proper or adequate treatment.

It was therefore with these thoughts in mind that a study of 260 cases, taken from the record rooms of two private Los Angeles hospitals, was undertaken.

STATISTICAL SUMMARY

There are 260 cases of proved endometriosis in this series which comprise all the known cases of endometriosis at two private Los Angeles hospitals from the period of May, 1930, to April, 1939. All of these women were operated upon and the diagnosis established or substantiated by pathologic examination of the removed tissues. Patients diagnosed clinically and not operated upon were not included. Cases diagnosed by the surgeon at the operating table, not substantiated by examination of removed tissue by the pathologist, were rejected. It is of interest that, in assembling the cases for this series, many cases of hemorrhagic ovarian cysts, diagnosed as endometriosis by the surgeon, were discarded, due to lack of pathologic confirmation. However, it was noted by the writers that in nearly every instance where dense adhesions were stated to be present, the pathologist was able to confirm a diagnosis of endometriosis.

These 260 women were operated upon by 63 surgeons. There were in this group of operators many general surgeons, a few gynecologists, and several general practitioners.

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TABLE I. INCIDENCE

Number of cases in series	260
Number of gynecologic laparotomies performed during this period	15,975
Per cent of proved endometriosis cases to all gynecologic laparotomies done	1.62%

A percentage of 1.62 is extremely low, and we believe does not represent a true incidence of endometriosis in this group of 15,975 gynecologic laparotomies. Most authors have estimated the incidence of endometriosis to be about one in ten. Two reasons for this apparently false percentage in our series present themselves. First, we have accepted only laboratory proved cases and have undoubtedly discarded many cases of true endometriosis. Second, our 15,975 laparotomies represent the work of numerous operators and undoubtedly many cases of endometriosis have failed of recognition.

CLASSIFICATION OF TYPES

For purpose of simplicity in the presentation of our statistics we have divided our cases into 3 types, as follows: (1) Internal or uterine type: Cases involving the uterus alone, the so-called adenomyoma. (2) External or pelvic type: Cases involving structures other than the uterus. (3) Combined type: Cases involving both uterus and pelvic structures.

We feel that the purposes of this paper can be better served by a simple division of cases such as the above, rather than a more complicated classification, as that of Newmann. In tabulating our statistics we have clearly distinguished between the internal or uterine type of endometriosis, the so-called adenomyoma, and the external or pelvic type. The treatment in these two major groups must be quite different. The external and the combined group (in which the uterus is involved in addition to other structures) tend to fall into one treatment group.

TABLE II. CLASSIFICATION OF TYPES

TYPE	NUMBER	PER CENT
Internal	129	49.6
External	95	36.5
Combined	36	13.9
Total	260	100.0

AGE INCIDENCE

Table III shows that the greatest incidence in our series was between the ages of 30 and 50 years, with the peak reached in the decade between 35 and 45 years. The fact that it does occur in the third decade and as late as the seventh must always be remembered. The youngest patient in our series was 21 years old and the oldest 63. Counsellor has reported a patient of 73 years of age.¹ The age incidence in our group corresponds closely with that of previously reported groups.

It is evident from a study of Table III and Fig. 1 that in our series adenomyoma was operated upon in a later age group than was the

TABLE III. AGE INCIDENCE*

AGE IN YEARS	DISTRIBUTION ACCORDING TO TYPE					
	INTERNAL		EXTERNAL		COMBINED	
	NO. CASES	PER CENT	NO. CASES	PER CENT	NO. CASES	PER CENT
15-19	0	0.0	0	0.0	0	0.0
20-24	0	0.0	2	2.1	2	5.5
25-29	7	5.4	17	17.9	4	11.1
30-34	13	10.0	33	34.8	5	13.9
35-39	25	19.3	22	23.2	9	25.0
40-44	35	27.1	11	11.6	8	22.2
45-49	31	24.0	8	8.4	7	19.4
50-54	14	10.9	1	1.0	1	2.8
55-59	3	2.3	1	1.0	0	0.0
60-64	1	0.8	0	0.0	0	0.0
65-69	0	0.0	0	0.0	0	0.0
Total	129	100.0	95	100.0	36	100.0

*Illustrating that the external or pelvic type of endometriosis is operated at an earlier age than the uterine type.

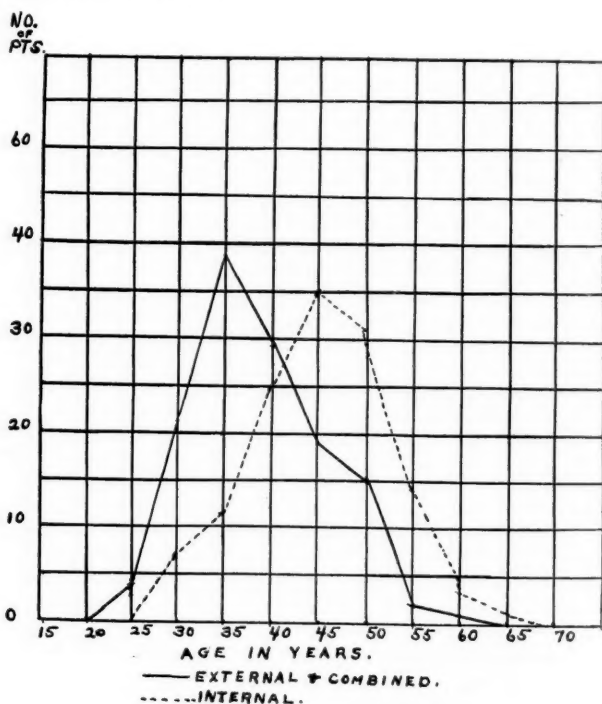


Chart 1.—Graph showing age incidence.

external type of endometriosis. At first glance this would seem to show that adenomyoma develops later in life than do the other types of endometriosis. However, it may well be that this apparent fact is false. It is possible that each type develops at correspondingly the same ages, but that adenomyoma is more slow in developing symptoms requiring surgery.

The external type of endometriosis in our series reaches its peak of incidence in the age group of 30 to 34 years; 75.7 per cent of all our cases

of this type were between the ages of 25 and 40 years. This fact presents a difficult problem in treatment. Most authors agree that ablation of all ovarian tissue after the age of 40 years in general pelvic endometriosis is indicated, but if three-fourths of the cases occur at earlier ages it would seem to be justifiable to operate radically at even an earlier age.

ORGANS INVOLVED

The anatomic distribution of lesions in this series follows closely that described by previous authors. Inasmuch as our series includes adenomyomas of the uterus, that organ was involved the greatest number of times, there being 162 such instances. The ovary showed the next greatest involvement, 84 lesions. There were 361 organs involved, many patients having double or multiple lesions.

TABLE IV. INVOLVEMENT OF ORGANS

ORGAN	NUMBER	PER CENT OF TOTAL ORGANS INVOLVED
Uterus	162	44.8
One ovary alone 53 }	84	23.2
Both ovaries 31 }		
Pelvic peritoneum	51	14.2
Rectovaginal septum	16	4.4
Bladder	11	3.0
Sigmoid	10	2.8
Fallopian tubes	6	1.6
Small intestine	5	1.4
Round ligament	4	1.1
Uterosacral ligament	3	0.83
Abdominal wall, p.o. scar	3	0.83
Appendix	2	0.56
Umbilicus	2	0.56
Infundibulopelvic ligament	1	0.28
Stump of cervix	1	0.28

ASSOCIATED PELVIC DISEASE

The relationship between endometriosis, fibromyomas, and endometrial hyperplasia has been described by Witherspoon and others.² Our series shows a high incidence of these lesions. Fibromyoma of the uterus occurred 108 times or in 41.5 per cent of our cases. In addition there were 17 instances where the pathologist diagnosed fibrosis of the uterus. These two lesions therefore total 125, or 48.0 per cent. The fact that less than half of these cases were of the internal or uterine type, as may be seen in Table V, is interesting, and again suggests the possibility of a common etiologic factor in fibromyoma and endometriosis.

Endometrial hyperplasia was diagnosed 28 times or in 10.7 per cent; while endometrial polyps were noted 21 times or in 8.0 per cent. These two lesions total 49, or 18.7 per cent; again an incidence considerably higher than could be found in any unclassified group of pelvic cases. It is quite likely that there were many other cases in our series in which there was an associated hyperplasia of the endometrium, particularly in the external type, because obviously no pathologic study was made of the uterus in many of these cases.

There was a high incidence of ovarian pathology other than that of endometriosis of the ovaries, there being 66 such cases or 25.0 per cent. The high incidence of menstrual disturbances, as will be shown later, may be due to this. Dysmenorrhea may be caused by any type of ovarian lesion, and it is possible that some of these cases of dysmenorrhea were due to associated ovarian pathology rather than to the endometriosis itself. Table V lists the number and types of pathologic lesions found associated with our cases of endometriosis.

TABLE V. ASSOCIATED PATHOLOGY

	IN- TERNAL	EX- TERNAL	COM- BINED	TOTAL	*PER CENT
Fibroid uterus	52	34	22	108	41.5
Ovarian pathology					
Simple follicular cysts	24	8	5	37	14.2
Lutein cysts	7	1	1	9	3.2
Inflammatory cysts	4	3	0	7	2.7
Multilocular cystadenoma	1	1	1	3	1.1
Hemorrhagic cysts (not choco- late)	1	1	0	2	0.8
Carcinoma ovary	0	2	0	2	0.8
Papillary cystadenoma	0	1	0	1	0.38
Dermoid cysts	0	1	0	1	0.38
Pseudomucinous cysts	0	0	1	1	0.38
Fibromas ovary	0	1	0	1	0.38
Fibrosis ovary	0	0	1	1	0.38
Granulosa cell tumor	1	0	0	1	0.38
Chronic pelvic inflammatory dis- ease	26	16	3	45	17.3
Endometrial hyperplasia	13	10	5	28	10.7
Chronic appendicitis	9	11	2	22	8.4
Endometrial polyp	12	3	6	21	8.0
Fibrosis uteri	10	5	2	17	6.5
Cervical polyp	2	0	1	3	1.1
Pregnancy, intrauterine	2	0	0	2	0.8
Carcinoma body uterus	2	0	0	2	0.8
Carcinoma cervix	1	0	0	1	0.38
Carcinoma bladder	1	0	0	1	0.38
Uterus bicornis unicollis	0	1	0	1	0.38

*Percentage computed on basis of number of cases. Therefore does not total 100 per cent because of multiple lesions.

SYMPTOMATOLOGY

A cardinal symptom of endometriosis is some disturbance of the menses. This may take the form of dysmenorrhea, menorrhagia, polymenorrhea, metrorrhagia, or frank uterine hemorrhage.

DYSMENORRHEA

Dysmenorrhea is a predominant complaint in our series. It was noted in 113 instances, or 43.4 per cent of the total number of cases. The distribution was as shown in Table VII.

It is apparent that dysmenorrhea was a more constant symptom in the general pelvic than in the uterine type of endometriosis in this series.

TABLE VI. SYMPTOMATOLOGY

COMPLAINT	INTERNAL	EXTERNAL	COMBINED	TOTAL
Menorrhagia	66	18	19	103
Metrorrhagia	23	17	12	52
Polymenorrhea	21	1	1	23
Uterine hemorrhage	3	1	0	4
Dysmenorrhea	40	54	19	113
Lower abdominal pain	34	44	12	90
Backache	24	9	2	35
Abdominal tumor (noted by patient)	10	11	5	26
Vaginal discharge	9	9	1	19
Bladder symptoms	7	4	2	13
Rectal pain	2	3	2	7
Postmenopausal bleeding	4	0	1	5
Gastrointestinal upsets	0	1	4	5
Dyspareunia	0	3	1	4

TABLE VII. DYSMENORRHEA

TYPE	TOTAL NUMBER OF PATIENTS	PATIENTS WITH DYSMENORRHEA	*PER CENT
Internal	129	40	31.0
External	95	54	56.7
Combined	36	19	52.7
Total	260	113	43.4

*Percentage computed according to each type. Therefore does not total 100 per cent.

EXCESSIVE UTERINE BLEEDING

One hundred and twenty-four patients, or 47.7 per cent, complained of excessive uterine bleeding, taking the form of menorrhagia, metrorrhagia, polymenorrhea, or any combination of these. These cases were distributed as shown in Table VIII.

TABLE VIII. EXCESSIVE BLEEDING

TYPE	TOTAL NUMBER OF PATIENTS	PATIENTS WITH EXCESSIVE BLEEDING	PER CENT
Internal	129	67	51.9
External	95	37	38.9
Combined	36	20	55.5
Total	260	124	47.7

As would be expected, in our series excessive uterine bleeding is a more frequent finding in the uterine type of endometriosis.

OTHER SYMPTOMS

The symptoms elicited in our clinical histories have been shown in Table VI. Lower abdominal pain follows menstrual abnormalities in frequency of occurrence. Bladder and rectal pain were not found to occur as frequently as has been stressed by other writers. The occurrence of 5 cases of postmenopausal bleeding, in each of which there was adenomyoma of the uterus, is interesting and important. Endometriosis has not been stated to be a cause of postmenopausal bleeding.

POSITION OF THE UTERUS

Position of the uterus could not be satisfactorily evaluated in this series. A retroposition of the uterus is believed to be an etiologic factor in endometriosis, other series showing a high incidence of retrodisplacement. In this series, in 127 instances, or 48.8 per cent, the position of the uterus was not stated on the record of the physical examination. Inasmuch as these were all pelvic cases (with the exception of the 3 cases of involvement of abdominal wall in postoperative scars) and a pelvic examination was done in every case, this omission seems to us to be a serious error and possibly explains some of the diagnostic pitfalls. Of the 133 stated cases 70, or 52.6 per cent, showed some type of retroposition.

PREVIOUS ABDOMINAL SURGERY

In compiling our statistics of previous surgical procedures we have considered only abdominal operations, because of the uncertainty of the records concerning vaginal procedures. Many of the patients stated in the history that they had had some type of vaginal operation, but were not sure as to whether it was a curettage, cauterization, or repair. While the number of patients who had had curettage of the uterus would be of interest, we felt that the figures would not be reliable, and therefore they were omitted. In tabulating abdominal surgery, we have distinguished between those cases in which the uterus, tubes, or ovaries were cut into (with the possibility of transplanting tissue of the endometrium, the endosalpinx or the ovarian cortex), and those in which other procedures were done. Ninety-six patients, or 36.9 per cent, had had a previous laparotomy.

TABLE IX. PREVIOUS ABDOMINAL SURGERY

TYPE	TOTAL NUMBER OF PATIENTS	PATIENTS WITH PRE- VIOUS LAP- AROTOMIES	PER CENT	PATIENTS WITH UTER- US, TUBES, OR OVARIES CUT INTO	PER CENT
Internal	129	53	41.0	34	26.3
External	95	29	30.4	15	15.7
Combined	36	14	38.6	6	16.6
Total	260	96	36.9	55	21.1

It would, from a study of this table, be difficult to draw any conclusion which would appreciably add weight to the theory of surgical distribution of endometrial tissue as an etiologic factor in the development of endometriosis. Almost as many in our series had other types of abdominal operations prior to developing endometriosis as had surgery which might be a cause of it.

TREATMENT EMPLOYED

The treatment of adenomyoma is simply a destruction of the lesion itself. This is accomplished usually by hysterectomy; less frequently by radiation. The cure of external endometriosis is not so easily accomplished, nor are surgeons so uniformly in accord as to the surgical indications.

All patients in this series were operated upon; as previously stated, only cases with diagnoses confirmed by examination of removed tissues being included. The terms conservative and radical are used only in relationship to the treatment of the ovaries. The surgery is tabulated as radical only if both ovaries were completely removed, any other surgery being considered as conservative, no matter what else was done. However, ovarian transplants, where both ovaries were removed from the abdomen and transplanted into the abdominal wall, must be considered as radical surgery. We feel that we are justified in this tabulation because of the short life of the transplant, which is thought to be about two years at best. Ovarian transplants were done in 9 cases.

Table X shows the incidence of conservative and radical surgery according to the type of endometriosis.

TABLE X. TYPE SURGERY EMPLOYED

TYPE ENDOMETRIOSIS	NO. CASES	CON- SERVATIVE SURGERY	PER CENT	RADICAL SURGERY	PER CENT
Internal	129	106	82.1	23	17.9
External	95	54	56.8	41	43.2
Combined	36	15	41.6	21	58.4
Total	260	175	67.3	85	32.7

We have made a study of the type of surgery employed in the various age groups of all those cases demonstrating external endometriosis.

TABLE XI. SURGERY IN VARIOUS AGE GROUPS

AGE	EXTERNAL ENDOMETRIOSIS		COMBINED ENDOMETRIOSIS		TOTAL			
	CONSERV- ATIVE	RADICAL	CONSERV- ATIVE	RADICAL	CONSERV- ATIVE	PER CENT	RADI- CAL	PER CENT
19-24	2	0	1	1	3	75.0	1	25.0
25-29	13	4	1	3	14	66.6	7	33.3
30-34	22	11	3	2	25	65.8	13	34.2
35-39	9	13	3	6	12	38.7	19	61.3
40-44	4	7	3	5	7	36.8	12	63.2
45-49	4	4	3	4	7	46.7	8	53.3
50-54	0	1	1	0	1	50.0	1	50.0
55-59	0	1	0	0	0	0.0	1	100.0
60-64	0	0	0	0	0	0.0	0	0.0
Total	54	41	15	21	69	52.6	62	47.4

In studying Table XI one cannot avoid assuming a critical view. When we consider external endometriosis where the ovary is the primary factor in controlling the disease, we must conclude that our surgeons have been too conservative, particularly in the older age groups. Our patients showing this external type total 131. Of these, 69, or approximately 53 per cent, were treated conservatively. There were 37 patients operated upon after the age of 40 years, and of this group 15, or 40 per cent, were left with ovarian tissue.

Resection of bowel was performed 3 times, twice of the ileum and once of the sigmoid. In neither case of small bowel resection was the diagnosis of endometriosis made at operation. The lesion was called in one case

"chronic inflammation of the terminal ileum," and in the other, "a scar at Meckel's diverticulum." Neither patient complained of nausea or vomiting, or exhibited any signs of intestinal obstruction. In the third case, there was a mass of endometriosis attached to the sigmoid. The operator stated that he could not easily separate this, and although both ovaries were removed, he did not feel that the endometrial mass should be allowed to remain. Consequently this mass, including a segment of the sigmoid, was removed and an anastomosis of large bowel done.

All of the above three patients survived the increased hazard of an intestinal resection, although the postoperative course of the patient, having the large bowel resection, was prolonged and stormy. It appears in reviewing these cases that bowel resection was not justified. Bilateral ovarian ablation would have effected a cure in each case.

DIAGNOSIS

Table XII presents a record of preoperative diagnosis, and of the diagnoses made with the abdomen open. It will be seen that there were only 6.9 per cent of preoperative diagnoses made. While this is admittedly small, we feel under no necessity to apologize. We believe that if similar statistical studies were made elsewhere they would be much the same.

We can find less excuse, however, for the fact that in only 106 cases, or 40.7 per cent, was the diagnosis made with the abdomen open. It seems that in spite of a voluminous literature on the subject, our surgeons are still not endometriosis conscious.

We feel that the statistics contained particularly in Tables XI and XII furnish ample justification for our study of endometriosis.

TABLE XII. DIAGNOSIS

Cases in series	260	-
Number diagnosed preoperatively	12	
Number suspected preoperatively	6	
Number either diagnosed or suspected preoperatively	18	6.9%
Number not suspected nor diagnosed preoperatively	242	93.1%
Number diagnosed at surgical table	89	
Number suspected at surgical table	17	
Number either diagnosed or suspected at surgical table	106	40.7%
Number not diagnosed nor suspected at surgical table	154	59.3%

MORTALITY

There were 2 deaths in this series, a rate of 0.77 per cent. Considering the gravity of some of the cases, we regard this rate as low.

One of these deaths occurred on the third postoperative day from paralytic ileus. The patient was operated upon for intestinal obstruction and massive endometriosis of the pelvis, with numerous dense adhesions in which loops of intestine were involved, was found.

The other death occurred on the thirteenth postoperative day. The case was one of adenomyoma with a submucous fibroid. The postoperative course was febrile and death may have resulted from postoperative infection. No autopsy was done.

FOLLOW-UP STUDY

A follow-up was attempted by means of a questionnaire addressed to all of our patients. Of the 258 sent out, a reply was received from 114 of them. The following study is based upon these replies.

Sterility and Marital Status.—Since the clinical history regarding the marital status, number of children, and sterility was inadequate we have relied entirely in this study upon replies to our questionnaires.

One hundred and two of these patients were married, or had been married. Twelve had never been married. Of the 102 married women 34, or 33.3 per cent, had had no pregnancies and may have been sterile.

TABLE XIII. MARITAL AND PARITY STUDY

	INTERNAL	EXTERNAL	COMBINED	TOTAL
Married	48	36	18	102
Not married	4	4	4	12
Married, no children	11	17	6	34

It will be noted in the figures above that the number of married women with pelvic endometriosis who had had no children is about double that of the married women with uterine endometriosis. The extent to which the reproductive function of the younger women treated by conservative surgery had been preserved, we are unable to estimate. Of the 114 women above responding to our questionnaire, only one had had a child since surgery. This was in the case of a woman, aged 32 years, married 7 years. At surgery both ovaries contained multiple small chocolate cysts, and there were endometrial transplants on the bladder. A partial bilateral oophorectomy was done, resecting the involved portions. The endometrial transplants elsewhere were excised where possible. Pregnancy followed twenty-seven months later. The patient is apparently well at present and has no symptoms of endometriosis.

RESULTS OF SURGERY

The 114 patients whom we were able to contact were asked to evaluate the results of the operation. Their tabulated responses appear in Table XIV.

TABLE XIV

	IN- TERNAL	PER CENT	EX- TERNAL	PER CENT	COM- BINED	PER CENT
<i>Results of Radical Surgery</i>						
Relieved entirely	13	81.2	17	100.0	10	90.9
Relieved largely	3	18.8	0	0.0	1	9.1
Relieved slightly	0	0.0	0	0.0	0	0.0
Relieved not at all	0	0.0	0	0.0	0	0.0
<i>Results of Conservative Surgery</i>						
Relieved entirely	32	88.8	13	56.5	7	63.6
Relieved largely	3	8.3	6	26.0	4	36.4
Relieved slightly	1	2.8	2	8.7	0	0.0
Relieved not at all	0	0.0	2	8.7	0	0.0

The above figures are, we believe, self-explanatory. While the results of radical surgery are apparently excellent, there are surprisingly few cases in the conservative group which are not largely relieved of symptoms. Of course only nine years have elapsed postoperatively for any patient in this series, and it may be that late sequelae may make the results less favorable, particularly in the conservative group.

It may be seen, however, that in our series the results of conservative treatment in pelvic endometriosis are distinctly of less benefit to the patient. When it is considered that of 37 patients past the age of 40, 40 per cent were treated conservatively; this must be considered either an error in recognizing the pathology, or an error in surgical judgment.

INTERESTING CASES

There were in our series two cases which are, we believe, sufficiently interesting to be presented in brief as follows.

CASE 1.—Mrs. D. A., white, female, aged 27 years, married, para 0, gravida 0. *Complaint:* Intermittent attacks of right lower abdominal pain. *Menstrual History:* Negative. No relationship between the pain of which she complains, and menstruation. *Surgery:* On March 31, 1939, an appendectomy and a suspension of the uterus were done. The uterus was described as normal, except as to position. Both tubes and ovaries were normal except that attached to the right tube was a small parovarian cyst. The appendix was bound down by numerous adhesions. *Pathologic Report:* Examination disclosed an unmistakable island of endometrial tissue within the meso-appendix. Repeated sections through the meso-appendix were cut and the same island was uniformly found in the same area. There was no possibility of this being an artifact, and it was believed that the island of endometrium had arisen from embryonic rest cells.

This case is apparently one of a single isolated, small endometrioma in the meso-appendix. No other areas of endometriosis were found in the pelvis or abdomen. We believe that this case may serve to illustrate the theory of embryonic cell rests.

CASE 2.—Mrs. C. C., white, female, aged 27 years, married, para i, gravida ii. *Previous Surgery:* Suspension of the uterus (modified Gilliam), and an appendectomy, 1929. Tubes and ovaries at that time were found to be normal, and there was no evidence of pelvic or abdominal endometriosis. *Complaint:* Pain and tenderness in right lower abdominal wall (at about the point of suture of the right round ligament in old Gilliam suspension of the uterus). Pain began shortly after operation and was worse at the time of menstruation. Patient could palpate a small lump in this area. *Diagnosis:* A diagnosis of endometrioma of right round ligament was made. *Surgery:* On Aug. 2, 1938, under spinal anesthesia, a hard, fibrous mass, cystic at certain points, and about the size of an acorn, was resected from the abdominal wall at the site of the old suspension stitch which approximated the right round ligament to the under surface of the right rectus fascia. Peritoneal cavity not explored. *Pathologic Report:* Confirmed diagnosis of endometrioma of right round ligament. *Follow-Up:* No symptoms had developed suggestive of pelvic endometriosis since surgery.

While we believe that no etiologic deductions are possible, this case suggests the probability of surgical transplant of tubal or uterine endometrial tissue.

SUMMARY

It will be repeatedly apparent in reviewing our statistics that this study was hampered by incomplete histories. Also accurate deductions as to results of treatment are impossible because we could contact less than 50 per cent of the cases in our series. However, we feel that certain facts brought out by our study warrant particular emphasis.

1. That adenomyoma becomes surgical at a later age than does pelvic endometriosis. This may be due to slower development of symptoms in the uterine site.

2. That the high incidence of fibromyomas and endometrial hyperplasia in our series would seem to add weight to a previously suggested common etiologic factor in these conditions and endometriosis.

3. That some disturbance of menstruation is the most commonly found symptom in our series. This takes the form of dysmenorrhea or some type of uterine hemorrhage.

4. That retroposition of the uterus was present in over half of our cases in which the position was noted.

5. That in external endometriosis the relief of symptoms was decidedly better accomplished by ablation of ovarian tissue than by conservative surgery.

6. That a much larger percentage of preoperative diagnoses are possible if attention is given to a more accurate history and if surgeons become as endometriosis minded as the incidence of the condition deserves.

7. That extensive endometriosis involving structures which render excision extremely hazardous, should be treated by removal of all ovarian tissue even in the younger age groups.

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PSEUDOUTERUS ARCUATUS AND FUNCTIONAL MALFORMATIONS OF THE UTERUS

THEIR EFFECT ON PREGNANCY AND PARTURITION

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CHANGES of contour in the normal pregnant and parturient uterus are encountered with sufficient frequency to warrant an inquiry into their significance. The textbooks of obstetrics make no reference to their mechanism or connotation during pregnancy and labor. A uterus arcuatus is a frequent malformation of the uterus. After labor the uterus returns to its normal contour. This type of uterus arcuatus is referred to as pseudouterus arcuatus and, with other temporary malformations of the uterus, is caused by a temporary incoordination of the uterus leading to functional malformations.

The human uterus is a midline organ, but has a bilateral origin. The uterus is formed by the fusion of the Müllerian ducts. The mesenchyme or muscle fibers are laid down on each duct and the muscle fibers interdigitate at the line of fusion on the anterior and posterior walls of the uterus. The blood and nerve supply of the uterus is bilateral. In the uterus simplex, the fused mesial wall of the Müllerian ducts are resorbed in a caudocephalic direction, and an arrest in the resorption of the fused mesial wall of the Müllerian ducts at different levels leads to the uterus septate or subseptate.¹

In the uterus duplex (rodentia), in which only the vagina represents a single midline birth canal, each uterus operates in labor as a single organ. However, some coordination between the two uteri is essential, for otherwise each uterus might expel a fetus into the vagina simultaneously, and produce a "traffic jam." This does not normally occur. In the bicornate uterus of the dog, for example, the lower portion of the uterus, which is analogous to the lower uterine segment of the human uterus, is fused. Thus, there must exist two types of coordinated activity in the uterus bicornis, namely, one to coordinate the activity between the two halves of the fused lower segment, and another between the fused lower segment and the two horns. If the first type of coordination did not exist, the two halves of the fused lower segment would not function simultaneously. If the second type of coordination did not exist, the two horns would empty simultaneously and the "traffic jam" would take place in the fused lower segment (corpus uteri). Thus, there exists in the anatomic bicornate uterus of the dog, a coordinating mechanism between the two fused halves and between the lower and upper (horns) segments. Thus, the two halves as well as the two segments of the uterus in the uterus bicornis are coordinated, at least during labor.

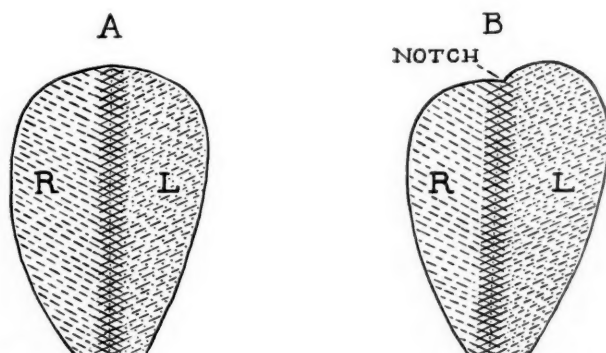


Fig. 1.—Schematic. A, Uterus with each lateral half (R and L) in equal tone. B, Uterus with left lateral half atonia (paresis or paralysis), while the right lateral half is hypertonic. Notch is the result of the change in tone of the two halves of the uterus at the mesial boundaries.

If ontogeny recapitulates phylogeny then the uterus simplex must possess the same coordinating mechanism, namely, one to coordinate the two halves and the other to coordinate the upper and lower segment. Observations on the uterus simplex of the monkey shows that such mechanisms physiologically exist, and must exist in order to prevent obliquity of the uterus or a sacculation of the upper or lower segment, or one of the uterine quadrants. If the various quadrants of the uterus were not coordinated, obviously a uterine contraction would not occur evenly throughout the uterus, and the uterus could not contract in one quadrant and relax in another simultaneously.¹⁻⁴

A disturbance of the physiology of the pregnant and parturient uterus may lead to difference in tone or strength of contraction of each lateral half of the uterus which would result in asymmetry. This will cause a lateral deviation of the uterus to one side of the abdominal cavity, which is called lateral obliquity of the uterus. A lateral obliquity of the

uterus may be associated with a "notch" on its fundal surface (Fig. 1, B). The lateral half of the uterus in normal or exaggerated tone is firm at its mesial fundal limit, while the other lateral half of the uterus is markedly atonic or paretic which causes the fundal portion to rise upward and produce a "notch." This would cause one to suspect an anatomic uterus arcuatus.

Clinical observations on the changes of the contour of the pregnant and parturient uterus demonstrate numerous malformations to be functional. A frequent functional malformation of the uterus is one which causes us to suspect the existence of an anatomic uterus arcuatus. I refer to such a malformation as pseudouterus arcuatus, until it is actually proved to be anatomic rather than functional. Functional malformations of the uterus may be present during pregnancy, may persist during labor, or may appear only during labor. Anatomic malformations exist in the uterus before labor, may or may not disappear during pregnancy and labor, and return during involution. The presence in the nonpregnant state is the only criterion of the existence of an anatomic malformation.

The functional malformations of the uterus are as follows: (1) Pseudouterus arcuatus and lateral obliquity of the uterus; (2) sacculations of the uterus with the following types: (a) sacciform dilatation, (b) *grosesse angulaire*, (c) Piskacek's sign; (3) irregular cervical dilatation.

Pseudouterus arcuatus is related to the lateral obliquity of the uterus. A lateral obliquity of the uterus is due to an incoordination of the uterus, resulting in atonia, paresis, or paralysis of a lateral half of the uterus, with a compensatory tonic contraction of the other lateral half of the uterus. The compensatory tonic contraction of a lateral half of the uterus is comparatively slight which permits the uterus to be deviated to either the right or left side of the abdominal cavity, but the fundus uteri presents a rounded outline, and is not "notched." The most frequent lateral obliquity of the uterus is to the right, but on frequent examinations of the contour of the uterus during pregnancy, will change to a normal midline symmetrical pregnant uterus, or to a left lateral obliquity of the uterus, or may return from the normal or left lateral obliquity of the uterus to a right lateral obliquity of the uterus. The intrauterine pressure does not change with the obliquity of the uterus. The lateral obliquity of the uterus may disappear with the onset of labor, or may persist for various periods of the labor (Figs. 2 and 3).

The pseudouterus arcuatus is usually associated with a lateral obliquity of the uterus. This functional malformation is due to the presence of a "notch" corresponding to the mesial aspect of the fundus uteri. The "notch" is caused by a marked tonic contraction of the upper portion of a lateral half of the uterus and an atonia, or paresis, or paralysis of the upper portion of the other lateral half of the uterus. In addition to the "notch" a vertical furrow may be palpated or seen on the upper mesial surface of the anterior uterine wall, extending downward from the "notch" for a short distance. The degree of changes of tone of the fundal portions of both lateral halves of the uterus will determine the degree of the pseudouterus arcuatus. The configura-

tion of the fundus uteri necessitates a differential diagnosis between a pseudouterus arcuatus and an anatomic uterus arcuatus. The intra-uterine pressure does not change with this type of functional malformation of the uterus. During the last trimester of pregnancy, a lateral half of the uterus may manifest tetany which necessitates a differential diagnosis of unilateral tetany, threatened rupture of the uterus, and abruptio placentae. I will present diagrams of pseudouterus arcuatus

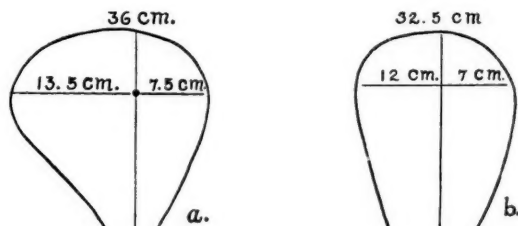


Fig. 2.—Right lateral obliquity of the uterus. *a*, Four weeks before the onset of labor. *b*, Two weeks before the onset of labor. With the onset of labor the uterus became symmetrical.

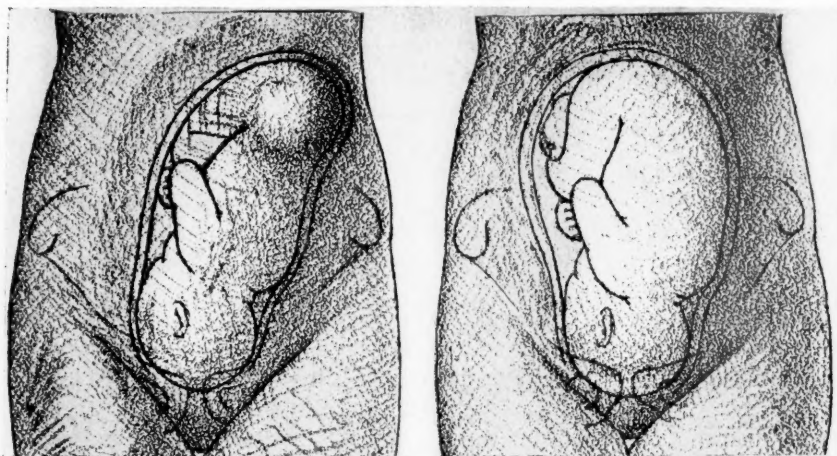


Fig. 3.—Uterus in left lateral obliquity and sacciform dilatation of the left upper quadrant of the uterus during the first stage of labor. With the second stage of labor the bag of waters was artificially ruptured which resulted in a normal functioning symmetrical uterus.¹

and no case reports, because the labor in my cases terminated normally, and during involution no anatomic abnormality was found (Figs. 4, 5, 6, 7).

Sacculation is a pouching or ballooning-out of a portion of the uterus. An incoordination of one segment or one or more quadrants leads to compensatory contraction of the uterus of the other uterine segment or quadrants.

Sacciform Dilatation.—A ballooning-out of an upper or lower segment is frequently observed. I have presented a case with a marked sacciform dilatation of the upper left quadrant of the uterus in labor

which persisted throughout the first stage of labor, but with the rupture of the membranes in the second stage of labor the sacciform dilatation disappeared and the uterus became symmetrical¹ (Fig. 3).

Sacculation of the lower pole of the uterus is frequently encountered in which the "obstetric" cervix uteri is found deep and posteriorly. The

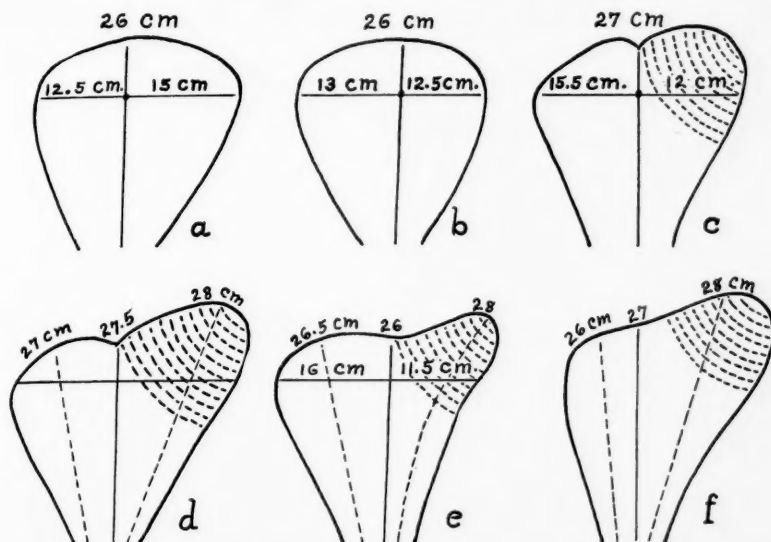


Fig. 4.—Primipara. Last menstruation October 22, 1930. Expected labor July 29, 1931. Contour of the uterus as: *a*, June 22. *b*, July 8. *c*, July 14. *d*, July 22, and roentgenogram showed a R.O.A., with the fetal spinal column deviated to the left. July 28 same as *d*. Uterus remained as *f* throughout the labor of seventeen hours and forty-four minutes. Delivery by outlet forceps and episiotomy.

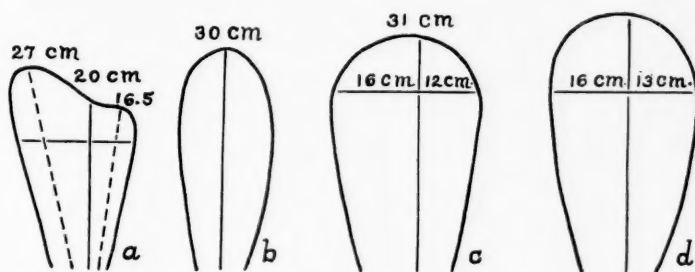


Fig. 5.—Frequent changes of the contour of the uterus during pregnancy. With the onset of labor the uterus became symmetrical.

posterior position of the "obstetric" cervix uteri and the ballooning-outward and forward of the lower pole of the uterus are due to a bilateral paresis of the anterior portions of the lower lateral halves of the uterus with compensatory contraction of the posterior portions of the lower lateral halves of the uterus. This explains the sacculation of the lower pole of the uterus and the posterior position of the "obstetric" cervix uteri.

Shaw⁵ reports a case that may be a bilateral ballooning of the fundus uteri. This occurred in a primipara, three months pregnant, in whom a cystic tender swelling was discovered on the upper portion of the uterus about the size of the uterus. The patient was laparotomized. The swelling proved to be a thin-walled sac of the uterine wall, and its cavity communicated with the uterine cavity by an opening which admitted two fingers. Both sac and uterine cavity were lined by the fetal membranes, and the fetus moved freely from one cavity to the other. This pathology appears to the author to have been a paresis of the upper portions of the lateral halves of the uterus, with the opening between the two uterine cavities as a tonic contraction of the physiologic retraction ring. The contents of the cystic and uterine cavities were removed, and the incision in the cystic cavity was sutured. The patient was laparotomized at a later date, the cystic cavity was not present, but a normal nonpregnant uterus was found. Bride⁶ described a similar case.

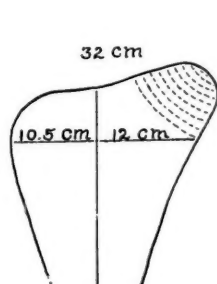


Fig. 6.

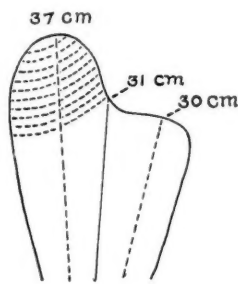


Fig. 7.

Fig. 6.—Contour of the uterus two weeks before the onset of labor. With the onset of labor the uterus became symmetrical.

Fig. 7.—Gravida ii, para i. First pregnancy showed no asymmetry of the uterus. Two weeks before the onset of labor the uterus showed a slight right lateral obliquity and a sacciform dilatation of the upper right quadrant of the uterus. With the onset of labor the uterus was found symmetrical.

Grossesse angulaire is considered to be due to the implantation of the fertilized ovum high in the cornual extremity of the uterine cavity. The placenta brings about the angular form of the uterus. I am of the opinion that the location of the placenta plays no role in grossesse angulaire, but is primarily due to a sacculation of an upper portion of a lateral half of the uterus. The angular form of the uterus is frequently found in the first four months of pregnancy. It corrects itself, and is followed by a normal pregnancy and labor.

On our service, we have seen two interesting cases of grossesse angulaire. The diagnosis was made of a grossesse angulaire, but on account of the severe pain on the side opposite to the sacculation the question arose as to a possible ruptured ectopic gestation. The two patients were laparotomized and an angular formed pregnant uterus was found. The abdomen was closed. The postoperative course was normal. The pain subsided with no other treatment than the use of sedation. Subsequent examination disclosed a symmetrical pregnant uterus. I have observed a number of similar cases of grossesse angulaire with severe pain on one side which on sedation disappeared and was followed by a subsequently normal pregnancy and labor (Fig. 8).

Piskacek's sign is interpreted by the author to be a mild type of sacculation of the upper portion of a lateral half of the uterus. It is not related to the presence of the placenta. I believe that it is a mild type of grossesse angulaire.

Irregular cervical dilatation is frequently encountered, and is usually associated with a lateral obliquity of the uterus. The normal functioning parturient uterus is associated with a synchronous and symmetrical dilatation of the lateral lips of the external os. When the uterus manifests a lateral obliquity, the uterine contractions of the atonic lateral half of the uterus do not undergo the same anatomic physiologic changes as the other half of the uterus. This brings about an irregularity of cervical dilatation. Or, one-half of the uterus is in the first stage of labor, while the other half of the uterus is in the second stage of labor.

Functional malformations of the uterus in my experience do not cause malpositions or malpresentations. The change of the form of the uterine cavity does not bring about a change of the intrauterine hydrostatic pressure. The fetus possessing a fetal postural mechanism accommodates itself to the form of the uterine cavity; the fetal form or ovoid does not change. A longitudinal position and presentation will become

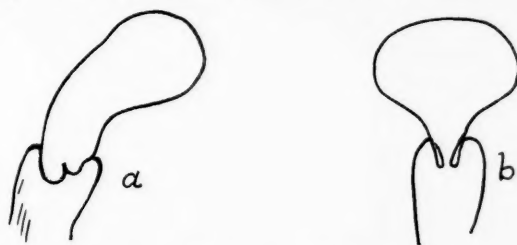


Fig. 8.—Multipara, pregnant about twelve weeks. Diagnosis: Grossesse angulaire and threatened abortion. Uterus in left lateral obliquity with marked tenderness on the right side. Twelve hours after the first examination the uterine colic subsided. Rectoabdominal examination showed a normal pregnant uterus. The pregnancy and labor which followed were normal.

more or less oblique, the presenting part may be high, or the presenting part may even rest in one of the iliac fossae, but the attitude of the fetus is not influenced by a functional malformation of the uterus. The author is convinced that a malposition or malpresentation results primarily from a disturbance of the fetal postural mechanism, but the mechanical factor plays a very minor role in these types of dystocia.⁷

THE DIAGNOSIS OF FUNCTIONAL MALFORMATIONS OF THE UTERUS

The presence of a "notch" on the fundal surface of the uterus, lateral obliquity of the uterus, sacculations, and irregular cervical dilatation during pregnancy and labor usually indicates a functional malformation of the uterus. If the malformation changes during pregnancy and labor, this change is practically pathognomonic of a functional condition. The presence of a "notch" on the fundal surface of the uterus per se does not indicate a diagnosis of uterus arcuatus. A "notch" is not characteristic of the uterus arcuatus of the monkey during labor. An abnormal contour of a lateral half of the uterus, or a segment of a lateral half of the uterus is characterized by a decrease in the tone of one-half or segment in comparison to the rest of the uterus by palpation. The contour of the uterus is transitory. The roentgenograms are of little value for the diagnosis. Only when the malformation persists post partum can the diagnosis of an anatomic malformation be made.

I have not kept statistics on functional malformation of the pregnant or parturient uterus, but am of the opinion that some form of functional malformation of the uterus may be found in nearly all pregnant patients, if the contour of the uterus is frequently looked for.

MANAGEMENT OF FUNCTIONAL MALFORMATIONS

The evidence presented demonstrates that these functional malformations are due to a disturbance of the physiology of the uterus. We have no means whereby we can correct this pathologic physiology of the pregnant and parturient uterus. Our management is empirical. An appreciation of the mechanism and the fact that the malformation is frequently self-limited indicates intelligent expectancy. Rupture of the uterus has not occurred in my experience in any form of functional malformation, and from a physiologic consideration, we need not fear this complication. Neither should we fear malposition and malpresentation. The treatment is governed by the conditions that actually arise.

CONCLUSIONS

1. The human uterus is a bilateral organ embryologically, anatomically, and physiologically.
2. The human uterus manifests bilateral synchronous and coordinated function.
3. Some degree of incoordination of each half of the uterus is not infrequently present during pregnancy and labor.
4. Pseudouterus arcuatus is due to an incoordination of the two halves of the uterus. The true or anatomic type of uterus arcuatus can be definitely diagnosed only post partum.
5. Lateral obliquity of the uterus is due to an incoordination of the two halves of the uterus.
6. Sacculation is due to a disturbance of a part of the upper or lower portion of each lateral half of the uterus.
7. Irregular cervical dilatation is explained on the basis of the incoordination of the two lateral halves of the uterus.
8. The management of functional malformations of the uterus is intelligent expectancy.

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AN EXPERIMENT IN CANCER CONTROL*

PRELIMINARY REPORT ON PERIODIC PELVIC EXAMINATIONS OF ONE THOUSAND WELL WOMEN

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THE percentage of uterine cancer cases which really are cured may be said to vary inversely with the stage of the disease in which the patient receives treatment.

This is well shown by a series of 50 consecutive cancers of the cervix treated on the Gynecological Service of the Woman's Medical College Hospital during the years 1931 to 1935 inclusive.

TABLE I. FIFTY CONSECUTIVE CASES OF CANCER OF THE CERVIX

GRADE	NO. OF CASES	FIVE-YEAR SURVIVALS	PER CENT
I	26	16	61½
II	9	3	33
III	11	0	0
IV	4	0	0

Since the organization of the American Society for the Control of Cancer in 1914 and the formation of the Cancer Committee of the Philadelphia County Medical Society in 1927, the women of this city have been told in season and out of season what the early symptoms of cancer of the uterus are, and that they should immediately consult their family physician if such symptoms appear.

If the members of this Society who practiced gynecology in Philadelphia before 1914 will recall the patients with cancer of the uterus who presented themselves before that date and will compare them with the patients who present themselves today, I am sure all will agree that the campaign to "Fight Cancer with Knowledge" has accomplished wonders. Nevertheless, in spite of this educational campaign, 321 women died of cancer of the uterus in this great medical center last year.

A consideration of these facts leads to the conclusion that cancer of the uterus may run its course for a variable length of time without causing symptoms which attract the patient's attention and that, if discovered in this early stage, the results of treatment might be different. In the hope that it might be possible to detect cancer of the uterus in this early and symptomless stage or that it might be possible to detect and eliminate lesions which predispose to the development of cancer, I decided to test the method of periodic pelvic examination on a large series of women.

*Read at a meeting of the Obstetrical Society of Philadelphia, January 4, 1940.

In this undertaking, I was encouraged by Dr. George E. Pfahler, Chairman of the Cancer Committee of the Philadelphia County Medical Society, by Dr. A. H. Estabrook of the American Society for the Control of Cancer, and by Dr. Ludvig Hektoen, Chairman of the Committee on Scientific Research of the American Medical Association. From this latter committee we received aid to cover the clerical expense of the Research.

My associates, Dr. Faith S. Fetterman, Dr. Margaret C. Sturgis, and I set about finding 1,200 white women thirty years of age and over who would volunteer to come for examination twice a year for five years. We transferred to this list our own patients who were already in the habit of coming for pelvic examination once a year. We transferred to the list patients from the postoperative follow-up clinic of the Hospital of the Woman's Medical College. We added to the list a few patients who consulted us for other than pelvic conditions and upon whom a routine pelvic examination was made. We recruited volunteers from women's clubs, from nurse alumnae associations, from social service organizations, and from the public at large as a result of the newspaper publicity given to the Research.

Each volunteer was given a leaflet describing the purpose of the research, stating that my associates and I had volunteered our services, and stating that if anything abnormal were discovered, a report would be made to her family doctor. In this connection, I should like to mention that the cooperation received from the family physicians has been most gratifying. While a few volunteers withdrew from the list stating that their doctors did not approve of this project, many more reported that their doctors were enthusiastically in favor of it.

As a result of the support that we have received from the volunteers and from their medical advisers, we are now in a position to report on the first and second examinations of a series of 1,000 women.

These examinations consisted in:

1. A careful bimanual pelvic examination
2. A careful inspection of the cervix in a good light
3. The application of Lugol's solution to the cervix according to the technique of Walter Schiller
4. The use of a blunt tipped pocket probe to detect friability of tissue according to the technique of Chrobak.

We did not use the colposcope, in the first place because we do not own one, in the second place because we wished to confine our tests to those that could be duplicated by the average general practitioner. At first quite a few biopsies were performed. As the experiment proceeded, we were more inclined to recommend the removal of cervical pathology in toto by means of surgery or conization.

In the first 1,000 examinations 4 malignancies of the uterus were found.

The first of these was in a woman 68 years of age. She had reported to Dr. Fetterman once a year for ten years for pelvic examination and had been transferred to the Research list. When she presented herself for examination she stated that she had noticed a spotting of blood for three days. The cervix was

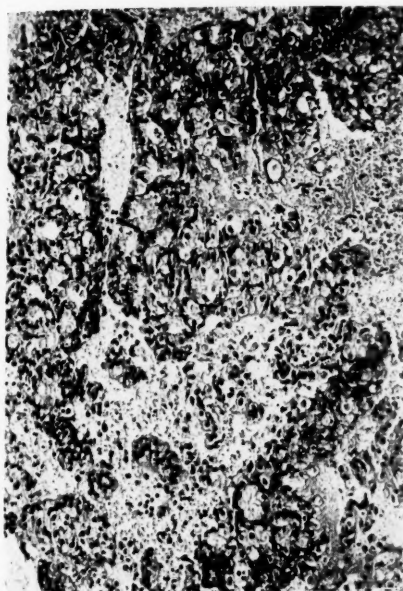


Fig. 1.

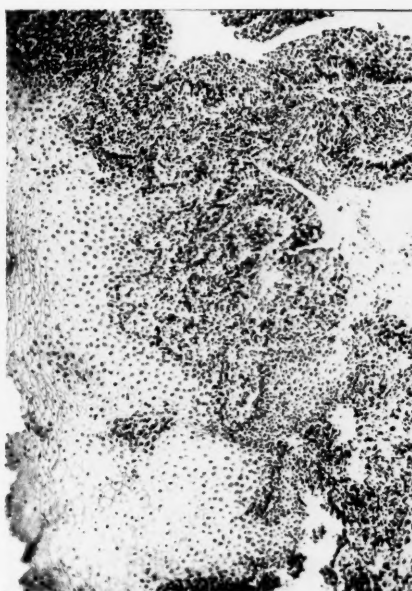


Fig. 2.

Fig. 1.—Curettings showing adenocarcinoma of the body of the uterus. (W. C. H. 43557.)

Fig. 2.—Squamous cell carcinoma of cervix found in tissue removed by biopsy. (W. C. H. 43433.)



Fig. 3.

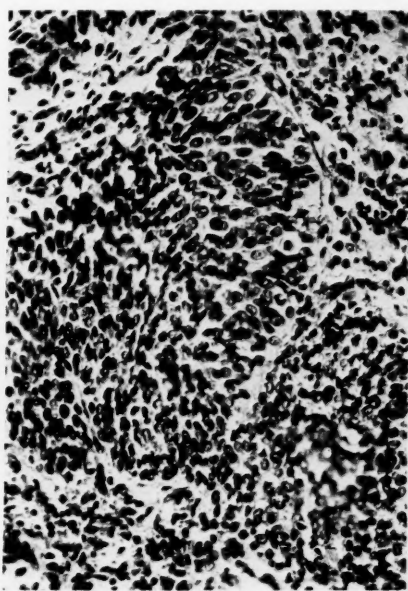


Fig. 4.

Fig. 3.—Squamous cell carcinoma discovered in a papillary erosion of cervix removed by Sturmdorf trachelectomy. (W. C. H. 46027.) (Low power.)

Fig. 4.—Squamous cell carcinoma of cervix discovered in papillary erosion removed by Sturmdorf trachelectomy. (W. C. H. 46027.) (High power.)

normal, and diagnostic curettage showed adenocarcinoma of the body of the uterus (Fig. 1). Since operation was contraindicated by various medical handicaps, radium and x-ray were used.

The second malignancy was found in a patient whom I had been asked to see on account of right upper quadrant pain. A routine pelvic examination showed a lacerated, hypertrophied, and eroded cervix. The Schiller test was negative. The probe sank in at one corner of the erosion. From this area a portion was taken for biopsy. In this tissue, Dr. Ingleby and Dr. Geiss found a small area of squamous cell carcinoma (Fig. 2). Radium and x-ray were used.

One of our volunteers asked that her mother and sister might be added to our list. The sister was found to have an extensive papillary erosion of the cervix which I excised by means of the Sturmdorf technique. I was surprised to receive word from the laboratory that a small area of squamous cell carcinoma had been found in the tissue removed (Figs. 3 and 4). Radium (4,050 mg. hours) was used.

A fourth woman came with a group of club women from a near-by suburb. Examination showed an extensive papillary erosion which was excised by the Sturmdorf method. Again to my surprise, Dr. Ingleby and Dr. Geiss discovered a small area of squamous cell carcinoma in the erosion (Fig. 5). Radium (3,900 mg. hours) was used.

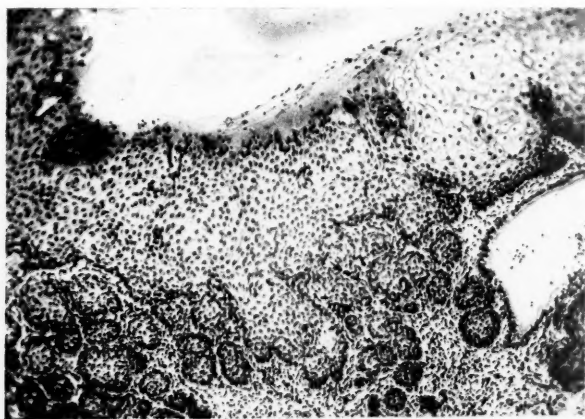


Fig. 5.—Squamous cell carcinoma of cervix discovered in papillary erosion removed by Sturmdorf trachelectomy. (W. C. H. 45989.)

In addition to these early malignancies, 357 benign lesions were found in 318 volunteers. These comprised:

Papillomas	1
Leucoplakic areas	6
Polyps	43
Endocervicitis and cervicitis	48
Inflammatory erosions	189
(Simple 50, papillary 53, follicular 1, not specified 85)	
Myomatous tumors	66
Ovarian cysts	4

Some form of treatment was recommended in 159 of these cases and was carried out in 113 cases. The procedures used were as follows:

Excision of leucoplakic areas	1
Excision of polyps	30
Cauterization of cervix	32
Conization of cervix	11
Surgical:	
Repair	7
Amputation	4
Sturmdorf	16
Not specified	7
Hysterectomy	5
Removal of ovarian cysts	2

Upon the second examination of these 1,000 volunteers, after an interval of six months, no malignancies were found. Old lesions were present in 177 women, 76 new lesions were found in 69 women. These new lesions comprised:

Leucoplakic areas	4
Polyps	15
Endocervicitis and cervicitis	19
Inflammatory erosions	24
(Simple 10, papillary 10, follicular 2, not specified 2)	
Myomatous tumors	14
Ovarian cysts	0

At this stage of our research, it is impossible to determine the real value of this undertaking. The first patient in whom malignancy was discovered would probably soon have found her way to a doctor whether she had come for periodic examination or not. The second case of malignancy might have lost some time before her doctor would have thought to examine her. The third and fourth malignancies had no pelvic symptoms except a moderate amount of leucorrheal discharge. It is highly probable that weeks or months would have elapsed before they reported this to their physicians.

The significance of the benign lesions which were discovered and the importance of treating them are debatable subjects upon which the pendulum of medical opinion has not yet come to rest. Since the earliest cases of cancer of the cervix that I have observed have always been found in areas of erosion or inflammation, I am of the opinion that these areas of chronic epithelial irritation predispose to the development of cancer. I, therefore, believe that the elimination of this type of cervical pathology is a wise and necessary procedure. I further believe that, in many cases, the only way to discover cervical pathology is by means of periodic pelvic examinations.

DISCUSSION OF ARTICLES ON PAGES 983 AND 995

DR. LEWIS C. SCHEFFEY.—It is noteworthy that in Dr. Macfarlane's series of 50 consecutive patients, 70 per cent were in Classes I and II. This is an unusually high percentage for anyone to see. In our experience, of nearly twenty years, from 1921 on, our Class I and II patients have ranged between 10 and 12 per cent.

She is to be congratulated on the unusually high five-year survival rate. The statistics she presents reveal no survivals in Classes III and IV, which means that it is the comparatively early case which makes up the reported survival rate of 38 per cent. Our salvage rate at Jefferson is about 16 per cent, all classes considered.

The four cancers discovered in the first 1,000 cases, and properly treated, have alone proved the value of Dr. Macfarlane's study. The recognition of benign lesions is of even more value, for I believe that the abnormal cervix predisposes to malignant change whatever may be the other factors concerned.

The plan of preliminary study outlined by Dr. Teahan and Wamock is complete and adequate. I am glad to see that the authors use the Schmitz classification. Anyone who has looked through Heyman's precise *Atlas*, relating to the League of Nations' classification of cervical cancer, will, I think, be carried away by the maze of detail encountered in attempting to follow it with accuracy. I would far rather talk to a colleague in the fairly simple terms of Schmitz, I, II, III and IV.

In our own work, we began with radium alone; later we used x-ray therapy after the radium. For the last three or four years we have been employing x-ray in the same dosage as Dr. Teahan, preliminary to the radium application. I am not, as yet, prepared to make any definite comparison regarding the use of preliminary x-ray prior to radiation with radium as compared with our former method. There are advantages and disadvantages. The advantages in using preliminary external radiation are that it will usually clear up the nasty, sloughing cervical lesion, reduce infection, and probably reach those cancer cells that are beyond the reach of radium used locally. However, it often happens that when one dilates the cervix afterward, preparatory to applying intra-uterine radium, he will find that underneath an apparently clean surface there is almost as much friability of the tissue as before the x-ray was administered. Also, the contracture which frequently results makes it more difficult to apply the radium in some instances.

The dosage of radium employed, about 8,000 mg. hr., with 1 mm. platinum screening, is a larger dose than we are giving at Jefferson. We limit our dosage to 3,600 to 4,500 mg. hr. dependent upon the extent of the lesion and the condition of the patient. Larger doses should theoretically be more effective, but we have experienced very severe reactions, local and general, from the larger doses.

I spoke about the fallacy of the five-year standard of survival. Recently I presented some interesting statistics from the Jefferson clinic which tended to show that a certain number of our survivors were living because of repeated radiation for recurrence, at varying intervals after the primary course of radiation therapy. Fifty-three per cent of the patients surviving from five to sixteen years had had a single course of radiation therapy, either with radium or x-rays, or a combination of the two, while 46 per cent had survived over an equal period because of repeated radiation therapy for recurrence at varying intervals after the primary course of treatment. Our survival rates are definitely influenced by re-radiations for recurrence, resulting from careful follow-up observations at regular intervals.

DR. CHARLES A. BEHNEY.—Cone irradiation has been employed by us for only fourteen months in treating about 30 cases. The cones vary in diameter to fit the vagina, and are similar to the cylindrical vaginal speculum except that they are made of lead-lined steel. They are circular, 50 cm. long, and fit on the x-ray tube so that the x-rays are delivered directly to the cervix without

passing through any intervening tissues. We have employed these in a small number of cases for only one year, and are unable to report results except to say that the immediate effect seems to be good, particularly in the advanced cases where one may be unwilling to apply radium locally.

May I add a word of appreciation for the first paper. We have known of this work for some time but until tonight were ignorant of the details and the result of this work at the Woman's Medical College Hospital. It emphasizes the need for greater stress on early diagnosis of carcinoma by frequent biopsy, both in our clinical practice and in our teaching. It is my conviction that further improvement in end results will be realized in this direction rather than by changes in therapeutic technique.

DR. HELEN INGLEBY.—I have here a diagram of a section of cervix showing an area of atypical cells with numerous mitoses, but no infiltration. Is this carcinoma? Further experience may give us the answer. This is not the same thing as a precancerous lesion. By a precancerous lesion is meant an area of cell proliferation, usually of inflammatory origin, which forms a suitable site for malignant growth. Growth may or may not supervene in a given case, but removal of such sites will probably prevent most if not all carcinomas in the cervix. Dr. Macfarlane in common with the majority of clinicians and pathologists holds that squamous or basal cell carcinoma of the cervix always arises in a previously diseased area. If she and they are right it follows that epithelioma of the cervix is preventable, not only in the majority, but in all cases.

DR. WAMMOCK (closing).—I wish to call your attention to the fact that of the histories of 229 cases which we have reviewed with reference to symptomatology, 80 per cent had bleeding in some form, leaving a total of 20 per cent without any bleeding. Of this number, some six per cent had advanced cancer before any sign or symptom appeared. During the year 1937, we discovered three Stage I cases by the use of the Schiller technique, referred to by Dr. Macfarlane. However, we do not rely solely upon this test. It is used as an adjunct to routine pelvic examination. Likewise, we do not use the colposcope.

As to the clinical grading, we prefer Schmitz' classification, which seems to be a very simple method. With reference to the dosage of radium in early cases, we feel that a large dose should be delivered if one expects to completely eradicate the cancer.

DR. TEAHAN (closing).—It must not be forgotten that the good results first obtained by irradiation in carcinoma of the cervix were obtained with radium alone. Theoretically, x-ray should be of value, for by its use more radiation reaches the broad ligaments. Practically, it is of value in some patients in cleaning up infection and making it easier to find the cervical canal.

Regarding re-irradiation with radium, with our dosage we practically never apply radium the second time.

DR. MACFARLANE (closing).—We have used the Schiller test systematically in our 2,000 examinations but feel that we have not derived much help from it. In fact, my associates and I feel that we derive as much help from a careful inspection of the cervix without Lugol's solution as with it.

A STUDY OF THE INCIDENCE OF SYPHILIS IN PREGNANT WOMEN AND SOME RESULTS OF THERAPY

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RECENTLY we made a determination of the incidence of syphilis in the patients seen at Duke Hospital. As a whole it was found to be 8.13 per cent. There was a marked disproportion between the white and colored patients. The incidence in white male patients was 2.7 per cent, and for the white female patients 3.2 per cent. In colored males the incidence of infection was 29 per cent and in the colored females 32 per cent. As can be seen from these figures, for the population group from which these patients were drawn, the incidence of syphilis in the colored race was roughly ten times that of the white race, and a greater incidence of syphilis was found in the females of both races. Because of this finding, we felt that a determination of the incidence of syphilis in pregnant women should be made because of its implications as a public health problem and as a problem of preventive medicine.

As a basis for this study the records of 2,152 unselected patients, all pregnant women, who were admitted during the years 1930 to 1938 to the obstetric wards, both private and public, of this hospital were examined.

The criteria employed for the diagnosis of syphilis consisted of either the laboratory finding of repeatedly positive blood serology and, in early seronegative syphilis, the finding of the *Treponema pallidum* on repeated dark-field examinations, or a definite history of syphilis for which no treatment or inadequate or insufficient treatment had been received with or without physical signs or stigmas of syphilis.

Blood serologic examinations were made routinely on all the obstetric patients at the time of their first visit to the prenatal clinics or at the time of their admission to the hospital, if no prenatal examinations had been made, and also in most cases serologic examinations were again made at the time of delivery. The serologic tests used were the Wassermann and Kahn reactions.

All of the patients diagnosed as having syphilis in the group on which this study was based were found to have a strongly positive Wassermann and/or Kahn reaction with the exception of 9 cases. Of these 9 serologically negative cases, 8 of the patients gave a definite history of syphilis and of having received some treatment prior to their pregnancy and 1 patient had dark-field, positive, seronegative, primary syphilis.

DATA

Of the 2,152 pregnant women whose case histories were studied, we found that 1,249 were white and 903 were colored. The incidence of syphilis in this group as a whole was 7.66 per cent as compared with an incidence of 8.13 per cent for the hospital patients as a whole. Only 10 cases of syphilis were found in the white group or an incidence of 0.8 per cent; whereas in the colored group, 155 patients

were diagnosed as having syphilis, giving an incidence of 7.6 per cent. The ages of these 165 patients found to have syphilis ranged between 16 and 42 years. Only 60 of them were primiparas. Most of them were from the lower economic brackets. The diagnosis of latent syphilis was made in 154 of the patients. Sero-negative primary syphilis was diagnosed in 1 patient and 6 of the patients were found to have secondary syphilis. Prenatal syphilis was diagnosed in 3 of the patients. One patient was found to have central nervous system syphilis.

Only 87, or 53 per cent, of the 165 patients received any antisyphilitic treatment during their gestational periods, and only 19, or 21 per cent, of the 87 partially treated patients received near the minimal amount of therapy which has been shown by the clinical cooperative studies⁴ to be necessary for the prevention of prenatal syphilis in the offspring of infected mothers. Of the 87 partially treated patients, 68, or 79 per cent, did not present themselves for diagnosis or treatment of their syphilis until after the sixth month of gestation. In 56 of the group of 165 syphilitic patients, the diagnosis of syphilis was not made until the patients were admitted to the hospital, usually in the first stages of labor. For various reasons, the remaining 22 patients in the group of 165 syphilitics failed to receive antisyphilitic therapy during their gestational period, or if some of them did receive treatment, we have no accurate statements in our records showing the time or amounts of such therapy.

Admittedly this group of patients constituted too small a number to allow the drawing of any definite conclusions as regards the true value of prenatal antisyphilitic therapy in the protection of offspring from infected mothers such as other investigations have shown it to be.¹⁻⁵ It was thought, however, that we could show by our studies that if some antisyphilitic treatment were given during pregnancy, and even though late in pregnancy and in amounts inadequate as compared to the amounts recommended by the clinical cooperative group studies,⁴ a more favorable termination of the pregnancy would result. It was observed that more full-term live births occurred in a group of patients who received some treatment during pregnancy than were found to occur in a group of patients who received no treatment, or who were inadequately treated prior to pregnancy. This concept has been expressed before in the writings of Moore,¹ McCord,³ Turner and McKelvy,⁶ Mitchell,⁷ and by Cole and others in the cooperative clinical studies,⁴ and perhaps by others.

We recognized that most of the patients studied had latent syphilis, and that many were also multiparas; both of which conditions have been shown^{1, 2} to play favorable roles in allowing full-term live births to occur even though the child so born may have prenatal syphilis. We were, however, dealing with similar patients in all the groups into which we had divided our patients for purposes of statistical classification, and since the terminations of pregnancy were so much better in those patients who received some treatment as compared with the untreated cases, we could not help but feel that the treatment caused these results.

This observation has been illustrated by dividing the patients into 5 groups with the results of the pregnancies being tabulated in Tables I, II, III, IV, and V. The terminations of pregnancies in 56 patients who received *no treatment either before or during pregnancy* have been shown in Table I. Table II was made to illustrate the terminations of pregnancy in 17 patients who received *some treatment before pregnancy, but none during pregnancy*. In Table III the terminations of pregnancy in 66 patients who received *some treatment during pregnancy only*

have been shown. In Table IV we have shown the terminations of pregnancy in 21 patients who received *some treatment both before and during pregnancy*. And in Table V the terminations of pregnancy have been tabulated in 5 patients who, we believe, had had some treatment, but about whom we could not obtain accurate information as to the amount or type of therapy.

TABLE I. THE TERMINATION OF PREGNANCY IN 56 SYPHILITIC WOMEN WHO RECEIVED NO ANTISYPHILITIC THERAPY BEFORE OR DURING GESTATION

ABORTIONS	MISCARRIAGES	PREMATURE	STILLBIRTHS	FULL-TERM LIVE BIRTHS
0	1	20	5	30
0	1.8%	35.7%	8.9%	53.6%

TABLE II. THE TERMINATION OF PREGNANCY IN 17 SYPHILITIC WOMEN WHO RECEIVED SOME ANTISYPHILITIC THERAPY BEFORE BUT NONE DURING GESTATION. AVERAGE AMOUNT OF THERAPY 3.1 GM. ARSPHENAMINE AND 0.5 GM. HEAVY METAL

ABORTIONS	MISCARRIAGES	PREMATURE	STILLBIRTHS	FULL-TERM LIVE BIRTHS
0	0	2		15
0	0	11.8%		88.2%

TABLE III. THE TERMINATION OF PREGNANCY IN 66 SYPHILITIC WOMEN WHO RECEIVED SOME TREATMENT DURING PREGNANCY ONLY. AVERAGE AMOUNT OF THERAPY 1.75 GM. ARSPHENAMINE AND 0.3 GM. HEAVY METAL

ABORTION	MISCARRIAGE	PREMATURE	STILLBIRTHS	FULL-TERM LIVE BIRTHS
0	0	5	1	60
0	0	7.6%	1.5%	90.9%

TABLE IV. THE TERMINATION OF PREGNANCY IN 21 SYPHILITIC WOMEN WHO RECEIVED SOME TREATMENT BEFORE AND DURING PREGNANCY. AVERAGE AMOUNT OF THERAPY 4.3 GM. OF ARSPHENAMINE AND 1.4 GM. HEAVY METAL

ABORTIONS	MISCARRIAGES	PREMATURE	STILLBIRTHS	FULL-TERM LIVE BIRTHS
0	0	0	0	21
0	0	0	0	100%

TABLE V. THE TERMINATION OF PREGNANCY IN 5 SYPHILITIC WOMEN WHOSE THERAPY, IF ANY, WAS NOT KNOWN TO US

ABORTIONS	MISCARRIAGES	PREMATURES	STILLBIRTHS	FULL-TERM LIVE BIRTHS
		1	1	3

At the top of each table we have shown the average amount of treatment received by each group to whom antisypilitic therapy was administered. These figures have been expressed as grams of arsphenamine and grams of heavy metal as determined by totaling the amounts received by each individual patient and then, by dividing by the total number of patients in each group, a general average was obtained. The therapy was expressed in this form for simplicity because, as

previously stated, we have not attempted to show the value of prenatal antisyphilitic therapy from the viewpoint of preventive medicine, therefore exact qualitative and quantitative expression of therapy has not been deemed necessary for our purpose. The arsenicals used were either arsphenamine or neoarsphenamine. The heavy metal was in nearly every instance bismuth of the insoluble form, as bismuth subsalicylate. The patients treated at clinics other than in this hospital may have received some mercury.

COMMENT

Certainly, the marked disproportion as found in the incidence of syphilis in female hospital patients as a whole as compared with the incidence found in obstetric cases is of some significance. Just how to explain this we do not know. One possible explanation of this observation may be that patients infected with syphilis are often at the same time infected with gonorrhea, and as is well known, gonorrhea frequently has disastrous effects on the female reproductive system with sterility as its aftermath. We have no statistics at present to support such a supposition, but hope later to attempt such a correlation. The social factor of marriage also must play some part in producing this disproportion.

The finding of a much higher incidence of syphilis in the colored women as compared to the white has been mentioned before by McCord.⁵ We believe this is a generally accepted observation. The reasons for this are probably many, such as economic status, social habits, environment, and racial habits. All of these factors are far too complex to go into in a paper of this type.

If our records are any indication of the general status of prenatal antisyphilitic treatment at other clinics, and if the prenatal treatment of syphilis is to assume its role as an ideal example of preventive medicine, an effort must be made to get pregnant women to physicians for prenatal care much earlier than most of our patients presented themselves. All that will be accomplished, otherwise, with inadequate prenatal antisyphilitic therapy, such as our patients received, will be to cause more pregnancies to terminate at full term with live births and thus probably to increase the number of prenatal syphilitics occupying their place in our already burdened social structure. In support of this idea that the late and inadequate treatment of pregnant syphilitic mothers may increase the number of children with prenatal syphilis, we found after examination of the records of 35 such children who have been receiving antisyphilitic therapy in the Pediatric Clinic of this hospital that 37 per cent of these patients were born of mothers who had received insufficient treatment late in their pregnancies. It is recognized that prenatal syphilis in itself is not hopeless from a therapeutic viewpoint, but when one sees the difficulty usually experienced in getting the mothers of these patients in for adequate treatment of their syphilis, and with the same recognized difficulty with their offspring, the picture does assume a rather foreboding atmosphere. At present in North Carolina attempts to prevent such a miscarriage of therapeutic endeavor are being made by appropriate

legislation. Recent laws have been passed requiring physical examination and serologic tests for syphilis of both partners prior to marriage.* A law which went into effect on Jan. 1, 1940 also requires all pregnant women to have a Wassermann or other approved serologic examination made.† If syphilis is diagnosed, treatment is mandatory.‡ Only future observations can show the true value of these laws. It would be of interest to study a similar group of patients within the next few years in this community to see if the recently enacted laws of this state will further the prevention of syphilis in unborn children as is expected of them.

SUMMARY AND CONCLUSIONS

1. The incidence of syphilis was found to be about one-fourth as great in the white and colored obstetric patients as it was found to be in the white and colored women patients admitted to the hospital wards and seen in the out-patient clinics of those departments other than obstetrics.

2. The incidence of syphilis was found to be roughly ten times greater in the colored women than in the white women both in the pregnant and nonpregnant groups.

3. More full-term live births were found to occur in the group of syphilitic mothers who received some antisyphilitic treatment, even if given late in pregnancy and in inadequate amount, than were found to occur in instances of pregnancy in the groups of syphilitic women who had received no treatment or who had been inadequately treated prior to pregnancy.

4. Most of the patients in our study were diagnosed as having syphilis late in their pregnancy, and consequently, antisyphilitic therapy was in most instances inadequate from the standpoint of preventing prenatal syphilis in their offspring by present accepted standards.^{1, 2, 4}

5. More effort should be made towards getting pregnant women to physicians for prenatal care during earlier periods of gestation than most of our patients presented themselves.

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‡Venereal Disease. Part I. Control and Treatment, Articles 7191 to 7198, North Carolina Code Annotated.

RESULTS OF TREATMENT IN CARCINOMA OF THE UTERINE CERVIX*

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THE uterine cervix is accessible for diagnosis and treatment. No other region tolerates more radiation. In spite of these favorable factors, the results obtained in the treatment of cervical cancer are poor. What is the explanation of this paradox? Many factors are involved, but there can be no doubt that the extent of the disease when cancer treatment is undertaken has more to do with the ultimate result than anything else. Until more women will cooperate and have periodic pelvic examinations, the extent of the disease when the patient begins treatment will probably be found to be affected more by the length of the interval between the appearance of the first symptom and the institution of cancer treatment than by any other single factor. Table I indicates the delay in 167 patients whose histories contain this information. From this it appears that, while the patient with carcinoma of the cervix is consulting a physician more promptly, there is still an average delay of two months between the time she visits her doctor and the time of her first pelvic examination. Failure to make a correct diagnosis after pelvic examination is generally due to a satisfactory biopsy not having been made. The delay between the pelvic examination and the beginning of cancer treatment has been found to be due to an incorrect diagnosis, disbelief on the part of the physician that cancer is curable, and unwillingness of the patient to face the facts and submit promptly to the necessary treatment.

TABLE I. AN ANALYSIS OF 229 CASES, 1928-1937

This shows the average time between the initial symptom, first examination, and specific cancer therapy, using 167 cases in which these data were included in the history. This material was assembled for an unpublished report by B. E. Wright, M.D., Jeanes Hospital, Philadelphia, Pa.

YEARS	NUMBER OF PATIENTS	TIME IN MONTHS		
		ONSET TO FIRST VISIT	FIRST VISIT TO FIRST EXAMINATION	FIRST EXAMINATION TO FIRST TREATMENT
1929-1931	29	7.76	0.58	4.06
1932-1934	55	5.73	2.84	3.51
1935-1937	83	4.57	1.88	3.41
Average	167	5.55	2.0	3.6

As far as the cancer itself is concerned, there are variable factors. It may be very virulent or radioresistant. The patient may have associated conditions such as diabetes, syphilis, fibroids, or pelvic inflammatory disease, which makes treatment more difficult.

*Read at a meeting of the Obstetrical Society of Philadelphia, January 4, 1940.

Finally, the cancer treatment may be improperly planned or executed. An incomplete operation may be performed, the correct diagnosis not having been made, or the extent of the disease not having been appreciated. When one is in doubt as to the amount of radiation to use, there is a strong tendency to use an insufficient amount.

During the past ten years, 1928 to 1937 inclusive, a total of 229 cases of carcinoma of the uterine cervix have been observed at Jeanes Hospital. Of this number, 136 patients seen before Dec. 1, 1934, have been observed for five years or more, and it is with these that we propose to deal. All patients have been followed. A total of 118 patients had microscopic verification. Of the remaining 18, some made only one dispensary visit, and in other instances treatment was considered inadvisable because of the extent of the disease or the patient's general condition. None of these 18 patients survived five years.

It is our practice to make a thorough physical examination on all patients. When carcinoma of the cervix is suspected, the patient is anesthetized, a bimanual pelvic examination is made, the cervical canal dilated, the depth of the uterus determined, and the presence or absence of pyometra noted. A biopsy specimen is taken, and finally a bimanual rectal examination is made. Cystoscopic examination is made on all patients, and where symptoms or extent of the disease suggest ureteral blocking, the ureters are catheterized. An x-ray examination of the lungs, lumbar spine, and pelvis is routine.

The lesion is classified clinically according to Schmitz.¹ One is not always satisfied by the classification given an individual patient because of difficulties encountered in estimating the exact extent of the disease. The 136 cases observed are classified in Table II. Of the three Stage I

TABLE II. CLINICAL STAGES

	CASES	PER CENT
Stage I	3	2.2
Stage II	10	7.3
Stage III	42	30.9
Stage IV	81	59.6
Total	136	100.0

patients, one was discovered following hysterectomy for a fibromyomatous uterus, and one also had cancer of the breast. From the figures in the table one notes that nearly 60 per cent fall into the advanced group, Stage IV. Another 31 per cent fall into Stage III, leaving less than 10 per cent in Stages I and II. It will be noted that no Stage V cases are listed. They are included in Stage IV due to our inability to determine whether the disease was recurrent or, what was more likely, had never been primarily controlled.

Table III shows the distribution of the patients according to the histologic type of the cancer cell found. Squamous and anaplastic types are the most common, constituting 75 per cent.

Except as above noted, our treatment has been exclusively by radiation. Until 1933, the radium radiation was patterned after Heyman's method of small doses repeated once or twice at two- to three-week in-

TABLE III. HISTOLOGIC TYPES OF CANCER

	CASES	PER CENT
Squamous	49	41.5
Anaplastic	39	33.0
Basal	18	15.3
Adeno	12	10.2
Total	118	100.0

tervals to deliver a total of 6,600 mg. hr. of radium. This was followed by a course of high-voltage x-ray treatments. The x-ray factors have remained constant and are as follows: 200 kv., 50 cm. STD, 30 ma., 2 mm. Cu and 1 mm. Al filtration, four ports, two anterior and two posterior, fields 15 by 20 cm. A dose of 200 r. is delivered to each port three times a week for a total of 2,400 r. units to each port. At the beginning of 1933 the method of treatment was changed, x-radiation being given first. Immediately following completion of the x-ray treatments, radium is applied within the uterus in a rubber tandem consisting of three capsules of radium, two of 13.33 mg. and one of 6.66 mg. filtered with 1 mm. Pt, and intravaginally in a colpostat, one 13.33 mg. tube in each arm, and one 6.66 mg. tube in a rubber capsule filtered with 1.5 mm. Pt is placed in front of the cervix to deliver a total dose of approximately 8,000 mg. hr. The patient is anesthetized and the radium is applied but once. The bladder and rectum are protected by gauze packing, and an indwelling catheter is inserted in the bladder.

According to Arneson,² this method of applying radium results in the greatest amount of radiation reaching the broad ligaments of any which he studied. According to him, it delivers 7 T.E.D. to a point 3.3 cm. on each side of the cervical canal. However, Sandler³ disputes Arneson's conclusions.

A comparative analysis of the two methods of application, even though the number of cases is small, will perhaps be of value. This is shown in Table IV. The apparent improvement may be ascribed to increasing

TABLE IV. CASES TREATED RADIOLOGICALLY*

	CASES SEEN	CASES TREATED	5-YEAR CURES	ABSOLUTE CURE RATE	RELATIVE CURE RATE	AVERAGE R. TO TUMOR	AVERAGE MG. HR.
High intensity radium radiation and high voltage x-ray treatment (1928-1932)	82	72	14	17.0	19.4	2,380	4,671
High voltage x-ray treatment and protracted radium radiation (1933-1934)	53	49	11	20.7	22.4	3,115	6,346
Total	135	121	25				

*The case treated by hysterectomy is not included.

dosage. The five-year survival as to the distribution of clinical grades is shown in Table V, indicating that Stages I and II have better than

TABLE V. FIVE-YEAR SURVIVALS, DISTRIBUTION ACCORDING TO CLINICAL GRADES*

	PATIENTS TREATED	FIVE-YEAR CURES	PERCENTAGE
Stage I	3	2	66.7
Stage II	10	6	60.0
Stage III	42	16	38.1
Stage IV	81	2	2.5
Stages I-IV	136	26	19.1

*This table includes the Stage I patient treated by hysterectomy.

50 per cent chance for cure, whereas Stages III and IV have about 15 per cent chance for cure. The five-year results are given in Table VI. Of a total of 136 patients seen, 122 were treated and 26 survived five years or more. The absolute cure rate is 19.1 per cent and the relative cure rate 21.3 per cent.

TABLE VI. FIVE-YEAR SURVIVALS

Total cases seen	136
Alive five years	26
Absolute cure rate	19.1%
Total cases with microscopic verification	118
Alive five years	26
Cure rate	21.1%
Total cases treated	122
Alive five years	26
Relative cure rate	21.3%
Total cases receiving primary treatment	69
Alive five years	23
Cure rate	33.3%
Total cases treated by combined x-ray and radium	51
Alive five years	19
Cure rate	37.3%
Total cases receiving secondary treatment	53
Alive five years	3
Cure rate	5.7%

Our total number of cases includes a large number of patients who have received treatment for cancer before coming to us, and we have therefore seen fit to separate these from those in whom we initiated the treatment. In 69 patients the treatment was instituted by us, and the five-year cure rate in this group is 33.3 per cent. Fifty-three patients had received treatment for cancer elsewhere, the disease either not having been controlled or having recurred. These patients were given more treatment, but only three survived five years, i.e., 5.7 per cent.

Not all patients have received combined x-ray and radium therapy. In some of the advanced (Stage IV) cases the use of radium appeared to be contraindicated. A total of 51 patients received the combined x-ray and radium, and the five-year cure rate in this group is 37.3 per cent. In this group, two patients developed vesicovaginal fistulas, one following Heyman's technique and the other following the Regaud method. Four fistulas occurred among patients receiving an incomplete

cycle of treatment. Ten fistulas occurred among those patients who had received their initial treatment elsewhere, and one in a patient receiving no treatment.

COMMENT

1. From a study of this group of cases, we believe that every patient with carcinoma of the cervix should have a thorough clinical investigation.

2. Treatment of such patients should not be undertaken unless all the personnel and facilities necessary for the treatment are available.

3. Except for the extent of the disease, the initial treatment is the most important factor in determining the ultimate result.

4. Inquiry as to extent of disease and the factors used at the initial treatment in some of the patients who have been referred for secondary treatment has disclosed a deplorable lack of information.

5. X-radiation should not be used as the sole method of treatment except in advanced cases where only palliation is to be expected.

SUMMARY

1. From Feb. 1, 1928 to Dec. 1, 1934, 136 patients with carcinoma of the cervix were seen. Of these, 122 were treated and 26 have remained well for at least five years, an absolute cure rate of 19.1 per cent and a relative cure rate of 21.3 per cent. With one exception, these patients were treated exclusively by radiologic methods.

2. The best results were obtained by combined x-ray and radium.

3. The interval between the appearance of the first sign and the patient's first visit to a physician averages five and one-half months.

4. The interval between the first visit to a physician and the first pelvic examination averages two months.

5. The interval between the first pelvic examination and the institution of cancer treatment averages three and one-half months.

6. There is an average delay of eleven months between the appearance of the first sign and the initiation of cancer treatment.

7. While the patient is consulting a physician more promptly after the appearance of the initial sign, there does not appear to be any shortening of the interval between the first visit and the first pelvic examination.

8. A large number of the patients were treated for cancer before coming to us and were given more treatment by us because the disease had not been controlled.

9. In 69 patients the treatment was initiated by us, and 22 of these lived five years or more, a cure rate of 33.3 per cent.

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(For discussion see page 988.)

THE PLACENTA IN TOXEMIA OF PREGNANCY

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ONE of the chief obstacles in all investigation and research in the problem of toxemia of pregnancy lies in making the diagnosis clinically. Because a patient has hypertension, edema, and albuminuria during the pregnant state does not mean that she has toxemia. Also because she has had essential hypertension, chronic nephritis, or pyelonephritis previous to the pregnancy, does not mean that she will or will not have the superimposed toxemia. In this paper toxemia of pregnancy refers to the effect of pregnancy, in certain cases, on the renovascular system resulting in hypertension, edema, and albuminuria. This is irrespective of the presence or absence of previous kidney or vascular damage. Clinically it is often impossible to make the above distinction as there is no clinical or laboratory finding available to prove the point. With this state of affairs in mind, we have been trying to differentiate the various hypertensive states by pathologic study, following the birth of the child.

Fortunately few of these women die and therefore pathologic diagnosis of kidney and liver lesions is rarely available. However, during the past twenty years we have gathered together a series of 24 autopsies¹ from our own and other hospitals in which we have made complete pathologic studies. From this group of autopsies, we have come to the conclusion that there is a definite kidney lesion which can be described as a glomerulonephrosis which is present in all cases of true toxemia. In contrast to previous reports, we have been able to find the characteristic liver lesion of hemorrhagic necrosis in only half of the cases. Therefore to us the kidney lesion seems the more important.

Due to the scarcity of autopsy material, some years ago we started studying the placenta as the only tissue available in most cases. We hoped to find some lesion typical of toxemia which would definitely classify the cases. We believed that we found such a lesion and reported it as such.² We have continued this work and still believe that we have a method of distinguishing true toxemia. At first we thought that we could distinguish between true toxemia and chronic nephritis. However, we soon discovered that some patients with chronic nephritis showed the lesion of toxemia and others did not. We, therefore, have come to the conclusion that we can distinguish between chronic nephritis and chronic nephritis with toxemia, but that all cases with or without previous kidney damage have the same placental lesion if they have the superimposed toxemia of pregnancy. Essential hypertension and pyelonephritis in pregnancy show no changes in the

placenta unless there is a superimposed toxemia. The characteristic placental lesion as previously described consists primarily of a premature aging of the placenta. As has been known for many years, the full-term placenta shows a certain amount of syncytial degeneration. This is normal and physiologic. On further investigation we found that this involved from 10 to 50 per cent of the small terminal villi. We then noticed that in toxemia the majority of the villi were involved and in the severe pre-eclampsies and eclampsies all of the small villi may be involved. In normal seven and eight months' placentas, there is little or no syncytial degeneration; but in seven and eight months' toxemic cases, there again was 50 per cent or more syncytial degeneration. The type of syncytial degeneration is quite characteristic. In its first stages it consists of the clumping together and autolysis of the nuclei in the syncytial cytoplasm (not the syncytial buds), leaving clumps of darkly-staining masses with no cell outlines and wide areas of syncytial cytoplasm without nuclei. The final stage is the disappearance of all nuclei from the syncytial layer, leaving the villus surrounded by a thin irregular layer of hyaline material. It is a lesion that can be easily recognized after sufficient study of normal syncytium. The type of fixation of the material, the stain and the thickness of the cut sections all affect the picture and therefore should be standardized before comparing the normal with the abnormal.

In addition to the above lesion we have noticed a marked congestion of the villus blood vessels in the toxemic cases. The blood vessels are distended with blood occupying most of the villus. The cause for this is hard to explain. Certainly if one regards the syncytium as similar in function to the glomerular epithelium of the kidney, the destruction of this epithelium plus circulatory congestion might easily explain the high fetal mortality in this condition. The lack of permeability of the damaged syncytium to products required by the fetus, including oxygen, might well injure the fetus severely.

With the above criteria in mind, we are now making a report on 100 cases of toxemia of pregnancy. We shall try and correlate the placental lesion with the clinical, laboratory, and endocrine findings available in these cases. We were very fortunate, in that, 60 of the cases in this series were studied in conjunction with Drs. Soma Weiss and Lewis Dexter of the Thorndike Memorial Laboratory. Their work³ consisted in observing the cases during pregnancy. Following delivery they made complete clinical and laboratory studies of these patients for the purpose of diagnosis and classification. They have kindly given us permission to quote some of their findings in this paper.

The first part of our study is shown in Table I. This is a comparison of cases classified by the placental lesions against the clinical findings of blood pressure, edema, and albuminuria. The outstanding point shown by the table is that the presence of albumin in the urine is most closely correlated with the placental findings. In 90 per cent of the 60 cases showing a definite placental lesion, albumin was present. In

all of the cases showing widespread placental damage, a large amount of albumin was present. Whether or not there is any relation between the physiology of placental degeneration and albuminuria cannot be stated. However, from this study, albuminuria seems to be the most important sign of the amount of toxic damage going on in the placenta. In the early placental lesions (40 cases), albumin appears in less than half. This would indicate that the placental damage begins before clinical signs of the condition appear. How closely related to the cause of the toxemia the placental damage may be, is hard to say, because there must be some factor causing the degeneration.

TABLE I

BLOOD PRESSURE	EDEMA	ALBUMIN*
<i>Definite Placental Lesion, 60 Cases</i>		
120-140	Slight or none	None
23%	23%	11%
140-160	Definite	S.P.T.
26%	51%	12%
160-240	Marked	H.T.
51%	26%	77%
<i>Beginning Placental Lesion, 40 Cases</i>		
120-140	Slight or none	None
42%	37%	55%
140-160	Definite	S.P.T.
37%	39%	25%
160-240	Marked	H.T.
21%	24%	20%

*S.P.T., slight possible trace; H. T., heavy trace.

Blood pressure in relation to syncytial degeneration does not seem to be nearly as constant as albumin. About one-half of the cases of true toxemia have a systolic pressure of 160 mm. of mercury or less; while one-quarter are under 140. This is also shown by the fact that 3 out of the 12 patients in this series with convulsions had a blood pressure of 140 or less. Of the 51 per cent of these patients with pressures over 160, the actual height of the blood pressure bore no definite relation to the actual condition of the patient. In the series of early cases the blood pressure averaged considerably lower than in the severe cases. However, over half of them were over 140 systolic and several of them ran as high as in the other series. These cases that ran a very high blood pressure with mild toxemia were largely of the group with previous hypertension. This is the point that is most confusing in the clinical judgment of these cases. If we had a basic blood pressure taken over a period of time previous to the pregnancy, it would be of immense importance. The rise in blood pressure during pregnancy is of much greater important than the actual level.

The amount of edema present is difficult to judge. As it depends upon the observations of different people, no standard can be laid down. Swelling of the feet and moderate swelling of the hands is so common as to be frequently disregarded. Edema in other parts of

the body is of more value, particularly of the face and abdominal wall. In this series there seems to have been somewhat more edema observed in the advanced than in the early cases. There are cases in both groups where edema was not observed and the amount of marked general edema seems to be about the same in both groups. Therefore edema is a somewhat vague observation and much less to be relied upon than the albuminuria.

Using our placental classification of toxemia, we have extracted several normal and toxic placentas for their content of prolan of pregnancy. We have also done urine extractions on the same contrasting groups. The findings are given in Table II. A survey of the figures

TABLE II

NORMAL PLACENTA*	PROLAN TOXIC PLACENTA	URINE PER 24 HOURS	
		NORMAL	TOXIC
4,000 R.U.	1,000 R.U. Eclampsia	200 R.U.	1,000 R.U.
2,500	540 Eclampsia	1,000	1,000
500	1,515 Eclampsia	1,000	1,000
500	1,000 Eclampsia	750	500
1,000	660	1,000	500
500	660	200	500
330	500	1,000	2,500
660	1,000	660	1,000
500	1,000	330	1,000
330	1,000		1,000
	660		1,000
			1,000
			500
			500
			1,000
			200

*R.U. per kilo wet tissue.

will show that while some normal placentas run a lower level of prolan than that of the toxic group, this is not always the case. Individual normal cases show even larger amounts of prolan than any of the toxic group and many of the toxic cases have as little as many of the normal cases. We have been unable to establish a definite level below or above which the prolan reading will show a normal or a toxemic case. In observing the urinary prolan we have found no significant difference between the total prolan of the normal and the toxic groups. This agrees with the work of Taylor and Scadran⁴ who were unable to demonstrate any constant increase in the prolan content of the serum or urine in toxemic cases. Smith and Smith,^{5, 6} have reported a higher prolan content in toxemia, as have other investigators.⁷ The difference in results must rest on the problem of what cases are truly toxemia of pregnancy. Until there is some generally accepted basis of classification contrary results will continue to appear.

A study of 60 cases of this series has been made by Weiss and Dexter.³ Their diagnosis was made following a complete medical and laboratory study with past history and follow-up. They have divided their cases in three groups as shown in Table III. Against their final diagnosis we have put out placental findings. The results are of considerable in-

TABLE III*

	TOXEMIA WITHOUT PREVIOUS HYPERTENSION 26 CASES	TOXEMIA WITH PREVIOUS HYPERTENSION 17 CASES	PREVIOUS HYPERTEN- SION UNINFLUENCED BY PREGNANCY 16 CASES
Placenta toxic	82%	96%	35% (borderline)
Placenta normal	18%	4%	65%

*From Weiss and Dexter.

terest. In the group of toxemia without previous hypertension, the diagnosis agreed in 82 per cent. The majority of the cases in which the placenta was found normal was in the borderline group with a very moderate rise in blood pressure and little or no albuminuria. This type of case is a very mild form of toxemia, if it be called such, and one would not expect to find any marked pathologic change. In the second group of toxemia with previous hypertension, the placental diagnosis was in marked agreement with the clinical one. This is important as it is this group of cases that offers the most difficult prognosis as far as their obstetric career is concerned. Finally, in the last group of cases, hypertension previous to pregnancy was established. From the medical point of view no toxemia was present during pregnancy. Some of these cases showed a high blood pressure and considerable albumin. They would be considered toxemic by the obstetrician. Yet their hypertension was present before and after pregnancy and the patient survived with no material change in her general condition. The answer to this cannot be settled as yet. It is important that in this group the majority with marked hypertension before, during, and following their pregnancy showed no toxic change in the placenta. This does show that in many cases pregnancy has little or no effect on the patient with previous marked hypertension. This observation is of great importance to the clinical obstetrician. The five cases of this group which showed toxic placenta were so borderline, both from the clinical and placental findings, that the diagnosis could have been made either way.

SUMMARY

A study of toxemia of pregnancy has been made with the purpose of correlating the placental pathology with the clinical and laboratory findings. Also a titration of the prolan of pregnancy in both the placentas and urines has been done. Sixty of the cases in this review have been studied by the medical service as well as the obstetric. From the results obtained, it is felt that the placental lesion is an accurate indicator of the severity of the toxemia. The placental lesion is found in cases with no previous hypertension or kidney damage. It is present in many cases with previous renovascular disease. Therefore, toxemia is an entity in itself which may either appear with an undamaged kidney or may be superimposed upon previous kidney damage. Albuminuria is the most accurate sign of the presence of placental damage. A titration of the prolan of pregnancy, both of the placenta and of the urine, shows no standard difference between normal and toxemic cases. The medical classification of hypertension in pregnancy agrees largely with the

placental findings except in some cases with previous hypertension in which there was a very early placental lesion with no marked clinical signs of toxemia.

CONCLUSIONS

1. Toxemia in pregnancy can be accurately judged by placental histology.
2. Albuminuria is the most trustworthy sign of the extent of the toxemia.
3. Toxemia is an entity present either with or without previous kidney damage.
4. Titration of the prolan of pregnancy is not an accurate sign of the presence of toxemia.

The authors wish to express their appreciation for the technical assistance of Miss Estelle L. Donovan and Miss Jean A. Berger.

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OBSERVATIONS ON THE PATHOLOGY OF TRICHOMONAS VAGINITIS AND ON VAGINAL IMPLANTS WITH TRICHOMONAS VAGINALIS AND TRICHOMONAS INTESTINALIS

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IN THE consideration of vaginitis with which trichomonas is usually associated, several important questions with reference to etiology, epidemiology, and pathology occur which still require investigation. Among them are:

I. What is the etiologic agent of the condition known as trichomonas vaginitis?

a. The most generally accepted belief is that *Trichomonas vaginalis* is the primary etiologic agent, although this contention has not been proved beyond question. It is based primarily on finding the flagellates in great numbers in the exudate and has not been subjected to exhaustive critical consideration.

b. A second theory considers that *T. vaginalis* is a commensal which multiplies rapidly in the suitable environment which is produced by some bacterium or other etiologic agent. A nonhemolytic streptococcus has been suggested by Hibbert (1933), Hesseltine (1933), and Hibbert and Falls (1938).

e. A third view indicates that trichomonas and some bacterium may both be responsible, one producing the initial tissue changes necessary and the other being a secondary invader.

II. What pathologic changes occur in the condition known as trichomonas vaginitis?

III. Is *Trichomonas vaginalis* a species distinct from *T. intestinalis*?

Similar questions have occurred with reference to the role of *T. intestinalis* in diarrheic conditions with which it is often associated. One opinion holds that it may be the cause of the diarrhea, while the other maintains that *T. intestinalis* is merely a commensal which appears in great numbers, because the environment is especially suitable for its rapid multiplication. The fact that carriers of the intestinal trichomonas also occur is used as evidence against the pathogenicity of *T. intestinalis*. On the other hand, kittens naturally infected with trichomonas have been found to exhibit dysenteric symptoms, and it also has been possible to induce diarrhea and dysentery in kittens by experimentally infecting them with *T. intestinalis* of man (Kessel, 1928).

Penetration of the trichomonads into the mucosa of the intestine was observed in some of the infected kittens, though such penetration was rare, a catarrhal-like inflammation with the presence of a diphtheritic membrane being the usual picture produced. Subsequent study of the intestinal mucosa of human cases positive for *T. intestinalis* has shown the occurrence of similar surface pathology but failed to show the presence of trichomonads within the tissue.

OBSERVATIONS IN THE PRESENT STUDY

Material utilized in the present study was collected from patients presenting symptoms answering to the clinical description of trichomonas vaginitis and from whom *T. vaginalis* was recovered.

The results of our observations may be considered under three headings.

1. *Pathology.*—The occurrence of an irritating frothy vaginal discharge often with an offensive odor was common to the cases considered in this study. Upon examination, the walls of the vagina were usually found to be injected and tender, presenting in some instances a pronounced hyperemia often exhibiting minute points of hemorrhage. In the more advanced cases granular areas were prominent.

Serial sections of biopsy material taken from these areas of hemorrhage and granulation were studied and show the following general appearance:

a. The surface mucosa in areas is covered with coagulated material in which trichomonads, leucocytes, and red blood cells are commonly found (Fig. 1). The surface epithelium is usually intact but in certain areas shows erosion with the migration of flagellates between the surface cells. Areas of hemorrhage are also occasionally observed to break through the surface epithelium.

b. In the subepithelial layer, areas of intense infiltration are found, consisting of lymphocytes, some polymorphonuclear leucocytes and a few plasma cells (Fig. 3). These areas show increased vascularity, extending in some instances to the basement membrane and in others to the surface epithelium.

c. In some instances definite necrosis appears within these areas of infiltration, the process extending toward the surface (Fig. 4). Usually it has not been possible to find trichomonads in these early areas of infiltration. In the areas which have become definitely necrotic (Fig. 5), it is often possible to find the flagellates (Fig. 2), and, in one case in which the mucosa had entirely eroded, they were seen between the cells in the subepithelial layer.

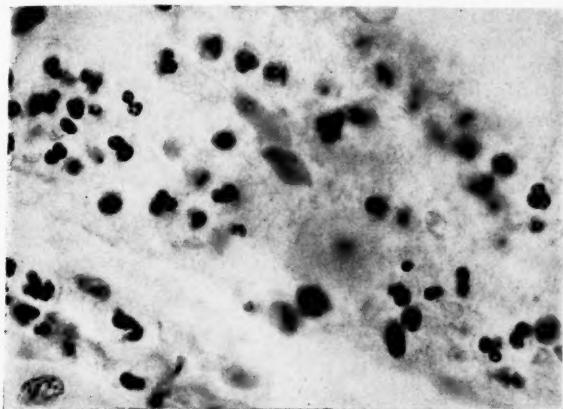


Fig. 1.—*Trichomonas vaginalis* in eroded surface mucosa.

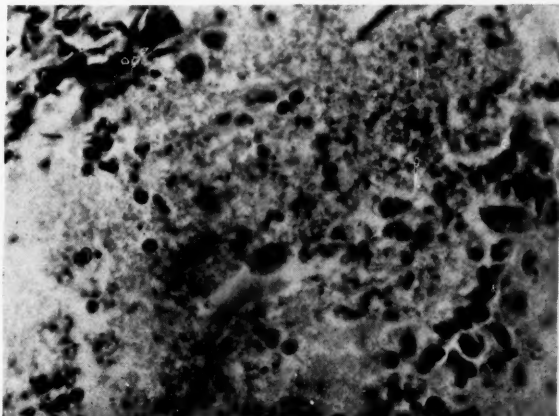


Fig. 2.—*Trichomonas vaginalis* in necrotic area. Enlarged lower area of Fig. 5.

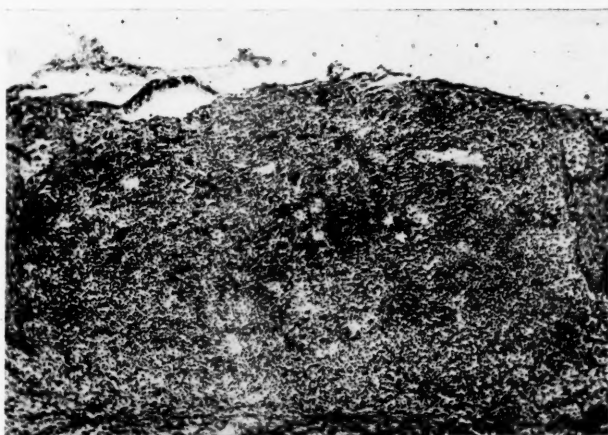


Fig. 3.—Early area of infiltration in subepithelium.

These findings indicate that the histopathology occurring in this type of vaginitis is not brought about alone by simple invasion of the flagellates from the lumen of the vagina but that there is some additional mechanism, either toxic or bacterial in nature which is responsible for the primary tissue changes or else that the flagellate is conveyed in some unrecognizable stage by the blood stream to the areas of infiltration and ultimate necrosis.

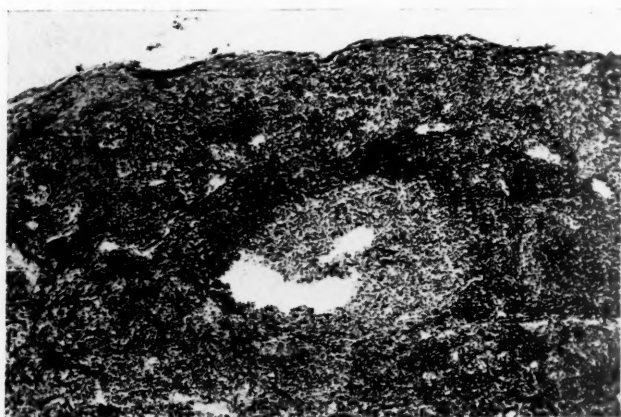


Fig. 4.—Later area of infiltration in subepithelium showing necrosis.



Fig. 5.—Areas of necrosis in subepithelium, the more advanced one showing presence of trichomonads.

2. Cultural Studies.—In order to look for some etiologic agent other than the flagellate and to compare the flora and fauna of normal vaginas with vaginitis cases, *T. vaginalis* exudates from cases of vaginitis and smears from normal vaginas were subjected to the following routine procedures: (a) Smear examination for trichomonas; (b) culture examination for trichomonas; (c) culture examination for fungi on Sabouraud's media; (d) culture examination on special media for: (1) members of the colon-typhoid-dysentery group of bacteria on eosin-methylene-blue plates, (2) streptococci in alkaline veal infusion broth, and (3) lactobacilli on whey agar; (e) stools from these patients were also examined for trichomonas.

Table I gives the results of these studies on 12 normal individuals and 33 vaginitis cases.

TABLE I. FAUNA AND FLORA OF NORMAL VAGINAS COMPARED WITH TRICHOMONAS VAGINITIS CASES

	NORMALS (12 CASES)		VAGINITIS (33 CASES)	
	+	-	+	-
<i>T. vaginalis</i>	0	12	30	3
Fungi	0	12	2	31
<i>Escherichia coli</i>	3	9	8	25
Streptococcus	12	0	33	0
Diphtheroids	12	0	33	0
Lactobacillus (Döderlein's bacillus)	7	5	3	30
After treatment			22	11
Stool examination for <i>T. intestinalis</i>	0	12	1	32

A. It will be observed that *T. vaginalis* was found in none of the normals in this series while it was found in 30 of the 33 who exhibited clinical vaginitis symptoms. The flagellate has been found, however, in a few instances in this study in which no characteristic vaginitis symptoms were apparent. These would represent the carrier state, which condition has been reported by other workers.

B. *Trichomonas intestinalis* was not found in the feces or vaginal smears of the 12 normals of this series and was found only once in the feces of the 33 patients who had trichomonas vaginitis. This flagellate is present in about 3 per cent of all stools examined in the Los Angeles County Hospital.

Four patients who harbored *T. intestinalis* examined during this period and who showed no signs of a vaginitis were examined for *T. vaginalis*. All were negative.

C. No fungi were found in the normal individuals and monilia was found only twice in the vaginitis cases.

D. No nonlactose-fermenting rods were encountered in either group, and *Escherichia coli* was found in 33½ per cent of each group.

E. Alpha streptococci similar in morphology to those commonly encountered in the intestinal tract (Kessel, 1936) but affording slightly different carbohydrate reactions were always present both in the normals and in the patients with vaginitis.

F. Diphtheroids also were present in both groups.

G. Lactobacillus, probably the same organism designated by some as Döderlein's bacillus, was recovered by culture from 7 of the 12 normals but only from 3 of the 33 clinical cases before treatment. After treatment and the disappearance of the clinical symptoms, this same organism was recovered from 66⅔ per cent of these individuals. This observation supports the opinion that the presence of aciduric bacteria may be used as an index of a healthy vagina.

These cultural studies indicate that *T. vaginalis* is usually associated with cases of trichomonas vaginitis but that no one bacterium or fungus isolated to date is associated more frequently with such vaginitis symptoms than with normal individuals.

3. Transmission Experiments.—Transmission experiments were of three types:

A. *Human vaginal implants as shown in Table II:** These were carried out on human volunteers whose vaginas were cultured both for bacteria and trichomonas prior to the implants. The series is small and does not warrant drawing final conclusions. It affords, however, some pertinent observations.

(a) All 3 cases into which exudate was implanted directly from cases of trichomonas vaginitis subsequently developed characteristic symptoms of vaginitis and two weeks after the implant *T. vaginalis* was recovered from them. Patients were treated after the fourth week.

*Observations in the current study support the view held by many observers and summarized by Wenrich and his coworkers (Bland and others, 1932) and Powell (1936) that morphologic differences exist between *T. vaginalis* and trichomonas from the intestinal tract. Trichomonads designated as *T. intestinalis* conformed to usual descriptions of trichomonas from the intestine and those designated as *T. vaginalis* to their description of this species.

TABLE II. VAGINAL IMPLANTS*

	NO. OF CASES	RESULTS			
		TRICHOMONAS		VAGINITIS	
		+	-	+	-
Direct smears from trichomonas vaginitis cases	3	3	0	3	0
Culture of <i>T. vaginalis</i> containing bacteria	3	3	0	2	1
Bacteria only	3	0	3	1	2
Cultures of <i>T. intestinalis</i>	3	0	3	0	3

*All cases negative symptomatically and negative for trichomonas by smear and culture before implants were made.

(b) All 3 cases into which laboratory cultures of *T. vaginalis* were implanted showed the presence of the flagellate in the vaginas two to four weeks after the implant. Only one, however, developed characteristic vaginitis symptoms. These cultures had been carried in the laboratory by frequent subculturing over a period of six weeks before the human implants were made. They contained the bacteria which remain stabilized in the protozoan culture which in this instance consisted of a gram-negative rod, of the escherichia group and an alpha streptococcus.

(c) A mixture of the above bacteria, free from trichomonas and of pure cultures of alpha streptococcus recovered from cases of vaginitis were implanted into three normal vaginas. One of these showed mild symptoms of vaginitis though no trichomonas were found. It should be noted that an occasional case of vaginitis, thought clinically to be trichomonas vaginitis, has been encountered in this study from which it has not been possible to recover *T. vaginalis*.

(d) Cultures of *T. intestinalis* were implanted into three normal vaginas. No trichomonads were recovered on follow-up examination two to four weeks later and no symptoms of vaginitis developed during this time.

B. Vaginal Implants in Monkeys: Since the reports of previous investigators on this topic are variable in their conclusions (see Hegner, 1928, 1929, 1934, Hegner and Chu, 1930, and Dobell, 1934), it was decided to attempt to transmit *T. vaginalis* and *T. intestinalis* to the vaginas of a series of 18 available monkeys belonging to the species *Macacus rhesus*. It was judged that the monkeys ranged from three to five years of age, all having begun the menstrual cycle. Notations were made at the first examination as to whether the animals were virgins or nonvirgins. The successful implants were obtained in 2 virgin and in 1 nonvirgin animal.

The feces of all monkeys were examined for *T. intestinalis* and all were found on the first or second examination to harbor this parasite. The vaginas of all monkeys were examined at least 5 times at intervals of one week before experimental implants of trichomonads were made and all were found to be negative for flagellates both by direct smear and by culture from each examination.*

The method used in taking the vaginal smears was: (a) to clean the region around the vagina carefully by washing and by subsequent swabbing with an alcoholic cotton swab, and (b) to insert sterile nasal forceps into the vagina and by means of a sterile cotton swab, dampened with saline, to swab thoroughly the vaginal wall. Smears and cultures were then made from this swab. Implants were made by injecting exudate or culture containing the trichomonads directly into the vagina by means of a pipette, and then holding the monkey's head downward for several minutes in order that the injected material might bathe the vaginal walls.

*Exceptions occurred in two examinations in which actual fecal material was found in the vaginas at the time of examination. Culture of this material yielded *T. intestinalis*, but when the examination was repeated three days later, the vaginas were negative for trichomonads.

A summary of the implants made and of the results obtained is found in Table III and may be summarized as follows:

a. Of 6 attempts to implant *T. vaginalis* contained in freshly collected exudate from a human case of trichomonas vaginitis to the vaginas of 6 monkeys, one produced positive results. The infection on the first and second weeks following the implant indicated marked multiplication of the flagellates which were found in great numbers among the epithelial cells from the vaginal wall. The third examination following the infection showed a marked decrease of flagellates, the same being detected by culture only. The fourth and subsequent examinations have demonstrated no flagellates. Subsequent implants of culture material containing *T. vaginalis* produced negative results with all 6 monkeys.

b. Of 6 attempts to implant *T. vaginalis* obtained from a human case of vaginitis and grown in Locke-egg serum culture media, into the vaginas of 6 monkeys, 2 produced positive results. The vaginal smears were heavily positive at the first examination one week after implant and have remained so for a period of twenty-eight weeks. No frothy discharge was apparent in the vaginas of these 2 infected monkeys though a marked cellular exudate was always present in the vaginal smears from these animals that was not observable in the uninfected monkeys. Two subsequent attempts to implant *T. vaginalis* from culture into the 4 negative animals of this series produced negative results.

TABLE III. ATTEMPTED IMPLANTATION OF *T. vaginalis* AND *T. intestinalis* TO VAGINAS OF *Macacus rhesus*

MATERIAL IMPLANTED	PREV. NEG. EXAMINA- TIONS	RESULTS		DURATION OF IN- FECTION
		+	- %+	
Exudate from <i>T. vaginalis</i> vaginitis	5 weeks	1	5	3 weeks
Culture of <i>T. vaginalis</i> from case of vaginitis	5 weeks	2	4	28 weeks
Culture of <i>T. intestinalis</i> from human feces	5 weeks	0	6	—
Culture of <i>T. intestinalis</i> from monkey feces	10 weeks	0	8	—

c. Attempts to implant cultures of *T. intestinalis* recovered from human feces into the vaginas of 6 monkeys produced negative results. Two repeated attempts were also negative.

d. Attempts to implant cultures of *T. intestinalis* recovered from monkey feces into the vaginas of 8 monkeys produced negative results. Five of the monkeys, however, have been used in experiment (c) and 3 in experiments (a) and (b) recorded above and suggest the possibility of immunity to infection, which subject requires further investigation.

In summarizing these experiments one concludes that: (1) attempts to implant *T. vaginalis* recovered from human cases of trichomonas vaginitis into the vaginas of 12 monkeys, negative for *T. vaginalis*, were successful in 3 or 25 per cent of the instances and (2) attempts to implant *T. intestinalis* recovered from man into the vaginas of 6 monkeys and *T. intestinalis* recovered from monkeys into the vaginas of 8 monkeys, all resulted in failure. (3) Sixteen attempts have been made using methods similar to those employed by Kessel (1928) in transmitting *T. intestinalis* of man to kittens. All met with negative results.

DISCUSSION AND CONCLUSIONS

Etiology of T. vaginitis.—The question of the etiologic agent of the clinical condition commonly known as trichomonas vaginitis is raised, and certain evidence is presented from studies of the histopathology and from implant experiments which indicates that the etiology of this condition is not as definite as is usually assumed and that some factor in addition to *T. vaginalis* may play a role in the production of clinical trichomonas vaginitis.

Early lesions in the submucosa fail to show the presence of trichomonads, while the later necrotic lesions often do.

Implants into normal vaginas of exudate from characteristic vaginitis cases which contained *T. vaginalis* and bacteria resulted in all instances in the occurrence of characteristic symptoms and in the recovery of the flagellates.

Implants of cultures containing *T. vaginalis*, *Escherichia coli* and an alpha streptococcus in one series and of these two bacteria in another, resulted in one clinical case of vaginitis in each series of three, though the case in which bacteria alone were implanted did not develop the characteristic severe symptoms ascribed to the usual case of trichomonas vaginitis.

Relationship of T. vaginalis and T. intestinalis.—Two conflicting opinions occur with reference to the relationship of *T. vaginalis* and *T. intestinalis*. (1) They are considered by some to be the same species and vaginal infections are regarded by some gynecologists as of intestinal origin. (2) By other workers they are regarded as different species, and it is considered that they cannot be transferred from the intestine to the vagina with facility.

In order to determine which of these theories is correct, it is imperative that conclusions be reached from studies made from the following approaches: (1) Morphologic comparison of the two organisms, (2) incidence of *T. vaginalis* in normal individuals and in cases of trichomonas vaginitis, (3) experimental implants of *T. vaginalis* and *T. intestinalis* to the human vagina, and (4) experimental implants of trichomonas in susceptible animals.

Observations in this study support the theory that *T. vaginalis* and *T. intestinalis* differ in several respects. Such conclusions are based on the following data:

1. They exhibit characteristic differences in general morphologic appearance and in their method of locomotion. Careful observations on this point have been made previously by Hegner (1925), Wenrich and his collaborators (1931, 1932), Stein and Cope (1931), Westphal (1935) and Powell (1936), and it would seem that any one who cares to look for the differences they record can observe them.

2. Incidence of *T. vaginalis* and *T. intestinalis* in nonvaginitis cases as compared with cases of trichomonas vaginitis. *T. vaginalis* has been consistently encountered in the vaginal smears of patients suffering from vaginitis while *T. intestinalis* does not show a higher incidence in the intestinal tract of vaginitis cases than of normals. Cases positive for *T. intestinalis* do not show an incidence of *T. vaginalis* higher than that reported in the general population.

3. *T. vaginalis* is easily transferred experimentally from one human vagina to another, while all attempts in this series of experiments to transfer *T. intestinalis* to the human vagina have resulted in failure. This is consistent with carefully executed attempts reported by others.

4. Attempts by previous investigators to implant trichomonads into the vaginas of monkeys have not met with uniform results. The earlier work of Hegner and his associates raises questions of interest but does not solve them. Hegner's last report (1934) indicates that *T. intestinalis* may live temporarily in the vagina of monkeys but that no evidence of multiplication was obtained. Dobell (1934) records a single instance of successful implant of a trichomonas from the human intestine into the vagina of a monkey. The infection in man was previously acquired experimentally from a monkey. Since Dobell does not state whether the trichomonas with which he was dealing was *T. vaginalis* or *T. intestinalis* (*T. hominis*) an accurate interpretation of his results is impossible.

The present report, using a larger series of monkeys than used by previous authors, supports the view that *T. vaginalis* of human origin may be experimentally established and multiply in the vaginas of monkeys and that *T. intestinalis*, either of monkey or of human origin may not be established in the vaginas of monkeys. The authors realize that even this series is too small to warrant the drawing of indisputable conclusions but feel that the results are significant.

5. *T. intestinalis* of man can be successfully implanted into the intestinal tract of kittens as shown by Brumpt (1925), Escomel (1926), Kessel (1926) and Bonestell (1936). On the other hand attempts to transmit *T. vaginalis* to the intestinal tract of kittens have resulted in failure in studies reported by Kessel (1933) and by Bonestell (1936).

The evidence reported in this study supports the theory that *T. vaginalis* and *T. intestinalis* (*T. hominis*) are distinct species, since they exhibit both morphologic differences and environmental differences. These data contradict the contention of some gynecologists that the trichomonads found in vaginas are of intestinal origin.

SUMMARY

Serial sections of biopsies from areas of hemorrhage and granulation in cases diagnosed clinically as trichomonas vaginitis are described. They indicate that the pathologic change occurring in this type of vaginitis is not produced alone by simple invasion of flagellates from the lumen of the vagina, but that some additional mechanism exists, either toxic or bacterial in nature which is partially responsible for primary tissue changes.

Implants into normal vaginas of exudate from cases of trichomonas vaginitis containing *T. vaginalis* and bacteria resulted in the occurrence of characteristic vaginitis, while implants of cultures of *T. vaginalis* and bacteria produced only one case of typical vaginitis and implants of *Escherichia coli* and an alpha streptococcus in culture produced only a mild vaginitis without characteristic discharge.

Experimental implants of *T. vaginalis* to human and monkey vaginas resulted in infection while attempts to infect human and monkey vaginas with *T. intestinalis* ended with negative results. These facts fail to support the theory that the trichomonads that infect the vagina are of intestinal origin.

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PREGNANCY AND COARCTATION OF THE AORTA

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THE term coarctation of the aorta implies a constriction of the vessel in the region of the insertion of the ductus arteriosus or its vestige. Bonnet has divided cases into infantile and adult types. In the infantile form there is a narrowing of the aorta between the origin of the left subclavian artery and the insertion of the ductus arteriosus, the region termed the fetal isthmus. In the adult type there is a constriction of varying degree about the insertion of the ductus.

In 1760 Morgagni called attention to the condition. In 1791, according to Barie, Paris described the first authentic case.

Blackford gives the incidence of coarctation of the aorta as approximately 1 in 1,550 cases as obtained from necropsy figures. At the time of publication of his 200 cases, only 19 had been diagnosed during life, indicating the frequency of overlooked diagnoses. In the various series reported there is a predominance of males over females in ratios varying from 2 to 1 to as high as 3 to 1.

Pathogenesis.—Several theories have been advanced relative to the pathogenesis of this condition. Those of syphilitic infection, thrombophlebitic propagation along the ductus, and ductal involution involving the aortic wall, have for the most part been abandoned. Syphilis is a rare associated finding and the disease could hardly occlude a lumen of such dimensions as the aorta. Brunner described ductal tissue joining that of the aortic wall and continuing into it but Walkoff failed to confirm this continuity. In coarctation, the finding that the ductus may be patent throughout or open at either end, made it obvious that ductal obliteration could not account for all cases. At present the most widely accepted theory is that of intrauterine anomalous development at the site of the fourth aortic arch as originally proposed by Rokitsansky and others. This is borne out by the finding of associated local and general anomalies.

Pathology.—Coarctation of the aorta occurs in varying degrees from an abrupt ligature-like constriction, to localized hypoplasia. The entire aorta is hypoplastic in about 10 per cent of cases. In rare instances the external configuration may be normal with complete occlusion of the lumen by stenosis or a membrane. Localized thinning of the wall with dilatation above and below the site of coarctation is described. Meixner's sections have shown destruction of the elastica with connective tissue replacement. Localized atheromatous and mycotic changes occur with occasional aneurysmal formation. The *Streptococcus viridans* is the

most common offending organism in the mycotic process. The collateral circulation depends on the anastomoses between the branches of the subclavian, aortic intercostal, and epigastric arteries, and the elaboration of anomalous vessels which would otherwise not have been called on to function. Tortuous dilated intercostal arteries erode the lower rib margins. In Abbott's series 18 out of 200 cases had associated cardiac anomalies, one of the most common being a bicuspid aortic valve of the developmental type found in 25 per cent. Cardiac hypertrophy was present in 75 per cent, most commonly involving all chambers and individually the left ventricle. Generalized vascular and somatic abnormalities are frequently associated. Cerebral aneurysms resulting from increased pressure on inherently defective vessel walls have been described by Turnbull.

Diagnosis.—This is based on the presence of all or some of the following: Evidence of collateral circulation, although this may be entirely absent clinically. Pulsating vessels may be found along the courses described, most frequently in the interseapular area where there may be a thrill and systolic murmur, the latter rasping in character, likened by Boehdalek to the placental souffle. Hallock has called attention to isolated suprasternal pulsations. Notching of the inferior rib margins may be seen on x-ray (Rösler's sign).

The coarctation may sometimes be visualized in the left oblique position. The aortic knob may be small or absent, and the ascending aorta dilated. In the upper extremities there is almost always a hypertension with high pulse pressure. King found normal pressure in the left arm and hypertension in the right which he attributed to the proximity of the left subclavian artery to the site of coarctation. In the lower extremities there is a relative hypotension with decreased to absent pulsations in the abdominal aorta and its branches. Bonnet has shown that these pulsations depend on the route taken by the blood in returning to the aorta rather than on the volume of blood flowing through them. If the blood is returned immediately by the intercostals the pulsations tend to be more pronounced. Blumgart has investigated the dynamics of the circulation. Ordinarily the pulsation in the femoral artery starts 0.01 second after that in the brachial artery, but where the blood follows a devious course this interval may be prolonged to 0.05 second. The blood supply to the lower extremities was within normal limits. It was pointed out that the arteriolar pressure in the legs could be raised only by elevation of the arterial pressure which depended upon increased aortic pressure above the site of coarctation, and this in turn could be accomplished only by increased cardiac work. Accordingly, one of the earliest symptoms of cardiac failure was intermittent claudication.

Grollman and Ferrigan studied cardiac output and found normal arteriovenous oxygen differences but a slightly increased cardiac output which they attributed to the increased metabolism.

Cardiac enlargement may be present. A long rasping systolic murmur may be heard over the entire precordium transmitted along the course of the aorta. Exophthalmic goiter is sometimes associated and has been attributed to the increased blood supply to the gland, resulting from the collateral circulation.

Essential hypertension, intrathoracic tumors, aneurysms, and exophthalmic goiter have been confused with coarctation of the aorta.

Prognosis.—The outcome of this condition presents a most disheartening picture. About 75 per cent of the patients die by their fortieth year, and, of these, about 75 per cent succumb to cardiovascular causes. There are isolated instances of individuals with coarctation surviving to the ninth decade. In Blackford's series 147 out of 196 died as a result of the lesion; 68 of gradual cardiac failure, 16 from sudden cardiac failure, 38 from rupture of the aorta, 25 from cerebral hemorrhage, and 6 from endocarditis or aortitis.

A survey of the literature has yielded 26 cases of coarctation of the aorta in pregnancy. Three additional cases are presented. The previously reported are summarized in Tables I, II, and III.

In the New York Lying-In Hospital, during the past seven years there have been three recognized cases of coarctation in approximately 31,000 obstetrical patients.

TABLE I. DEATHS DURING PREGNANCY OR SHORTLY THEREAFTER

AUTHOR	AGE	PARITY	GRAVIDITY	COL-LATERAL CIRCULATION	BLOOD PRESSURE	CARDIAC EN-LARGEMENT	EKG	NOTCH-ING RIBS	PERIPHERAL PULSATATIONS	OUTCOME
Fawcett	45	viii	ix	--	--	+	--	+	--	Death from cardiac failure 14 days post partum. Autopsy revealed complete atresia of aorta at insertion of patent ductus, fused aortic valves, thin atheromatous aortic wall
Strassman	25	i	ii	+	--	+	--	--	--	Death from rupture of aorta at end of pregnancy. Autopsy revealed dilated aorta with smooth intima, aortic valves thickened
Kreigh	28	ii	iii	+	--	+	--	--	--	Hemiplegia in seventh month and death from another cerebral accident in ninth. Autopsy revealed moderate stenosis of aorta at insertion of obliterated ductus and hypoplastic proximal aorta
Katz	25	i	ii	--	--	0	--	--	--	Death from rupture of aorta into pericardium at end of pregnancy. Autopsy revealed extreme stenosis at insertion of patent ductus, dilated aorta with smooth thin walls, and normal valves
Hallock and Hebbel	31	v	vi	+	--	0	LAD	0	--	Death from endocarditis several months following normal delivery. Autopsy revealed moderate stenosis with mycotic aneurysm above, bicuspid aortic valves covered with fresh vegetations, splenic and renal infarcts

TABLE II. CASES IN WHICH PREGNANCY HAD A DELETERIOUS EFFECT

AUTHOR	AGE	PARITY	GRAVIDITY	COLIAT- ERAL CIRCUL- ATION	BLOOD PRESSURE	CAR- DIAC EN- LARGE- MENT	EKG	NOTCH- ING RIBS	PERIPH- ERAL PULSA- TIONS	OUTCOME
Weinberg and Gartenlaub	38	i	ii	+	RA 130/100 LA 240/120 RL 150/100 LL ?	+	LAD	+	Decr.	Fainting attacks and bedridden for 6 months after first pregnancy; then well for 8 years until second pregnancy when she developed precordial pain, dyspnea and thyrotoxicosis which persisted after normal delivery. Subsequent thyroidec- tomy with some relief
Eppinger and Midelfart	28	0	ii	+	RA 300/125 LA 290/130 RL 135/100 LL 110/90	+	LAD	+	Decr.	Cerebral accidents, precordial pain, epistaxis, ver- tigo, headaches, scotomas, dyspnea and fainting during pregnancies both resulting in abortions
King	25	ii	-	--	RA 122/66 LA 122/60 RL 104/90 LL 108/90	0	Neg.	0	Decr.	Severe throbbing headaches during both preg- nancies
King	24	0	i	+	A 160-210 90-100 L 110-140 70-80	0	--	+	--	Precordial pain and dyspnea since childhood, worse during pregnancy. Blood chemistry and renal function normal. Low forceps delivery, normal puerperium. Told to avoid further pregnancies
Maxwell	34	iv	v	+	Arm 245/160	--	--	--	Decr.	Dyspnea and ankle edema since childhood. Seen in fifth month with aggravation of above plus head- ache, scanty urine and albuminuria. Improved with bed rest, subsequent course not given
Laffont and Laffargue	24	ii	iii	--	--	+	--	--	Decr.	Edema and severe dyspnea fourth month, miniature section and tubal sterilization. Febrile course requiring digitalis. No signs of cardiac failure one month later.
Lian, Abaza and Frumusan	19	0	i	+	--	+	Neg.	+	Decr.	Dyspnea after onset of pregnancy and severe at- tacks of syncope. Therapeutic abortion third month. Course not given
Lian, Abaza and Frumusan	30	0	i	--	--	+	--	+	--	Cardiac failure following birth of child. Course not given

TABLE III. CASES WITHOUT EVIDENCE OF UNTOWARD EFFECT OF PREGNANCY

AUTHOR	AGE	PARITY	GRAVIDITY	COLLATERAL CIRCULATION	BLOOD PRESSURE	CARDIAC ENLARGEMENT	EKG	NOTCHING RIBS	PERIPHERAL PULSATIONS	OUTCOME
Strassman	57	vii		+	--	+	--	-	---	Found dead from cardiac failure. No history of obstetrical difficulties. Autopsy revealed complete stenosis, smooth intima, and normal valves
Gossage	53	xiii		0	--	0	--	-	Present	Suffered a hemiplegia many years after last pregnancy. Course not given
Weber and Price	56	xi		+	220 190	+	--	-	---	Death from rupture of aneurysm in neck. No past obstetric difficulty. Last pregnancy 12 years previous. Aorta showed atheromatous changes
Leudet	37	iv		+	--	+	--	-	Deer.	Death from rupture of aorta. No past obstetric difficulties. Extreme stenosis of aorta without dilatation or atheromatous changes
Abbott	38	i		-	--	-	--	-	---	Death from congestive failure. No obstetric difficulty
Brunner	30	i		+	--	0	--	-	---	Death from pulmonary tuberculosis. Pregnancy one year previous without difficulty. Aorta obliterated by internal septum below insertion of patent ductus. Proximal aorta hypoplastic with atheromatous changes. Valves normal
Blackford	22		i	+	RA 168/94 LA 164/90 RL 102/88 LL 98/84	0	Neg.	-	Deer.	Miscarriage at 6 months without previous symptoms. Diagnosis confused with exophthalmic goiter. Course not given
Haberer	47	vii		+	--	+	--	-	---	Death from complications of transverse myelitis resulting from pressure of dilated artery. No past obstetric difficulties. Complete stenosis of aorta at site of obliterated ductus. Dilatation of proximal aorta. Bicuspid aortic valve
Van den Berg	29	iv		+	250	+	--	-	Deer.	No obstetric difficulties. Course not given
Evans	45	ii		+	A 205 120 L 85/7	+	--	+	Absent	Shortness of breath, precordial pain, hyperthyroidism, dilated ascending aorta. No past obstetric difficulties. Course not given
Hamilton and Stewart	22		i	+	--	+	--	+	Deer.	Uneventful pregnancy and labor. Course not given
Troutman	45	ii		+	A 160-120 90-100 L 85/7	+	Neg.	+	Absent	Choking and dyspnea while under observation. One miscarriage. No obstetric difficulties. Course not given
Caballero	31	iii		+	A 210 90	+	--	+	Absent	Two previous abortions. No obstetrical difficulties. Course not given

The first patient, R. P., a 26-year-old white primigravida, with a negative Wassermann and a funnel typical contracted pelvis, was first admitted in the fourth month of pregnancy for study of cardiac condition discovered at the initial clinic examination when signs of mild cardiac failure were noted. The past history was unremarkable except for dyspnea and palpitation on effort for six years. She had never suffered precordial pain or leg cramps. The patient showed some cyanosis and moderate dyspnea. There was marked evidence of collateral circulation. There was a soft blowing apical systolic murmur, and a loud harsh systolic murmur at the base. No diastolic murmurs were heard. Blood pressures RA 140/74, LA 130/80, not obtainable in the lower extremities. There was a marked temperature difference in the upper and low extremities. Chest film showed scalloping of the ribs and cardiac enlargement in the region of the left ventricle. The electrocardiogram showed normal sinus rhythm, rate 111, PR 0.16, QRS 0.07, no deviation of electrical axis, split QRS, split R₁ and R₂, T₁ and T₂ positive, and T₃ negative. Strayhorn has previously reported the case with detailed studies on cardiac function. As pregnancy progressed, the heart sounds became louder, the basal murmur louder, and the pulsations in the collateral vessels more pronounced. There was an increase in cardiac output out of proportion to the increase in oxygen consumption. The cardiac output fell just before term and returned to normal post partum. The patient was carried to term under strict regimen of limited activity and a classical cesarean section done under open drop ether with delivery of a 3,500 Gm. living infant. Sterilization was not performed. Palpation of the abdominal aorta during operation revealed the vessel to be of normal dimensions but only very feeble pulsations were felt. During operation the blood pressure dropped considerably but returned to former levels within a few hours. The section was done primarily because of fear of rupture of the aorta. Follow-up studies one month post partum revealed improvement in symptoms which had increased during the pregnancy. The physical signs were less marked. The electrocardiogram showed definite left axis deviation. Six months post partum there was no evidence of cardiac failure.

The second patient, E. B., a 23-year-old white primigravida, with a negative Kline reaction and normal pelvis, was admitted for study in the thirtieth week of gestation because of hypertension and history of known heart disease since the age of 5. She had had dyspnea on exertion for many years, recently aggravated by the pregnancy. There had never been precordial pain or leg cramps. Examination revealed the patient to be free of any distress. A systolic thrill was felt over the base. A loud systolic murmur was heard over the entire precordium, transmitted intensified along the course of the aorta down the back. There was no clinical evidence of collateral circulation. Blood pressures: RA 138/75, LA 135/70, RL 120/90, LL 115/90. On x-ray the heart was enlarged to the left. There was no notching of the ribs. The aortic knob was small. The electrocardiogram showed a tendency to left axis deviation. During the remainder of the pregnancy there was an increase in dyspnea and ease of fatigability. After a four-hour labor, the patient was delivered spontaneously of a 3,040 Gm. living infant. Renal function tests and blood chemistry during the puerperium were normal. Follow-up studies ten weeks post partum revealed that the patient tired very readily and felt unduly weak. She had no chills, fever, or precordial pain. For the first time a diastolic murmur was heard at the base transmitted down the left sternal border. Blood pressures RA 135/80, LA 130/60, RL 110/80, LL 100/80. There were no petechiae. Liver and spleen were not palpated. The development of the diastolic murmur suggested the following possibilities: damage to the aortic valve, stretching of the aortic ring, damage to the aortic wall, or formation of vegetations on the valve.

The third patient, R. Z., a 27-year-old Maltese primigravida, with normal pelvis and negative Kline reaction, was admitted for study of hypertension noted at initial clinic visit in the fourth month of pregnancy. Past history was entirely negative. Examination revealed evidence of collateral circulation, attenuation of the retinal arterioles, cardiac enlargement to the left, a harsh systolic murmur audible over the entire precordium and transmitted down the back over the course of the aorta. A bruit was heard over the pulsating vessels in the scapular region. Blood

pressures: LA 230/110, RA 200/100, LL 125/110, RL 125/110. X-ray revealed enlargement of the left ventricle and scalloping of the ribs. Electrocardiogram revealed left axis deviation. Renal function tests and blood chemistry were normal. Because of the strong desire of the patient to bear children and the relatively advanced stage of the pregnancy, the patient is being carried to term under a strict regimen of rest and limited activity. At term delivery will be effected by cesarean section and tubal sterilization performed under open drop ether.

DISCUSSION

There are, in all, 29 patients with an average of about 3 children each. Five died during pregnancy or soon after delivery: 2 from ruptured aorta, 1 of cardiac failure, 1 of cerebral accident, and 1 of endocarditis. Ten patients surviving pregnancy were definitely made worse by it. In other words, in slightly over half of the cases reported (including ours), pregnancy evidently had a deleterious effect upon the condition.

It is apparent that patients with coarctation are in constant danger of sudden death or serious accident. As has been pointed out, there is a bicuspid aortic valve in 25 per cent of cases and the same is found in 50 per cent of cases with rupture of the aorta. The pathologic thinning of the aorta and other arteries, particularly the cerebral, has also been pointed out. Once the diagnosis is confirmed, unless the patient shows evidence of cardiac failure, the clinical findings are not necessarily related to the immediate prognosis. As has been stated, the sword of Damocles is constantly over the head of these unfortunate patients. The findings of the condition at autopsy in individuals dying suddenly may be a complete "surprise d'amphitheatre." Besides the vulnerable points listed above, the congenital lesion is a *locus minoris resistentiae*, and all chances of infection should be strictly avoided.

There can be little doubt that the strain of pregnancy and labor may either aggravate the condition or cause sudden death. Examples of both have been given above. If pregnancy can occur and maintain itself, it seems logical to assume that either the coarctation is slight, or if extensive, the collateral circulation must be adequate so that in each instance the uterus receives an ample supply of blood. It should be stressed again, however, that sudden death may occur in either instance.

Stander and Cadden found that the cardiac output increased 50 per cent in pregnancy, beginning about the fourth month. Cohen and Thomson found increase in cardiac output up to the ninth lunar month with subsequent decrease prior to labor at term. Therefore in the second and early third trimesters of pregnancy, one may expect to have the increased cardiac output of pregnancy superimposed on that of coarctation. This may aggravate a pre-existing strain or impose a new one. Although one may expect some lightening of this burden toward the end of pregnancy, the stress of labor may be too much for a thinned aorta or cerebral artery. Already defective valves may be further damaged.

The work of Goldblatt and others has indicated the role of the kidney and renal blood flow in the genesis of hypertension. Ryland and Steele have shown that decreased renal blood flow in coarctation of the aorta is the most likely cause of the associated hypertension. By clamping the aorta proximal to the renal arteries in dogs, Steele was able to produce

an increase in diastolic pressure in the femoral as well as the carotid artery. Pregnancy is known to increase the renal burden and may thereby aggravate the underlying condition.

SUMMARY

Coarctation of the aorta is discussed and the literature surveyed with regard to pregnancy complicated by this condition. Three additional cases are analyzed. Evidence is presented to show that pregnancy adds to the risk in patients with this condition.

CONCLUSIONS

Pregnancy and labor present definite risks to patients with coarctation of the aorta. Therefore contraception is indicated in this condition. In patients presenting themselves early in pregnancy, therapeutic abortion is definitely indicated. If pregnancy is far advanced and interruption from below not feasible, delivery should be effected by cesarean section and sterilization performed. In isolated instances it may be desirable to carry a patient a short time to viability of the infant with full knowledge of all the risks involved.

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MENSTRUAL ENDOMETRIAL BIOPSY

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IT IS generally recognized that endometrial specimens can be obtained as a simple office procedure, without the need even for local anesthesia, and devoid of any practical risk, in all cases in which a thorough curettage is not necessary. Such specimens have become indispensable in the diagnosis of various types of menstrual difficulties and in sterility studies.

For these purposes one usually wishes to secure the specimen as near an expected menstrual period as possible, to note the evidence of corpus luteum activity, and if present, its degree. The secretory changes in the endometrium are a late interval occurrence, and probably continue to the beginning of menstruation. Consequently the nearer the onset of menstruation the specimen is obtained, the more accurately does the endometrium reflect the endocrine factors as they actually exist.

However, even in menstrual cycles which are considered to be "regular," there is usually a normal variation; thus the twenty-eight-day cycle may vary between twenty-six and thirty days, and sometimes more than this, in women who have no complaints. Ovulation time doubtless varies between certain limits in succeeding cycles in the same woman, also the interval between ovulation and the height of corpus luteum activity, and between this time and the beginning of menstruation.¹

Because of these variations, one does not know, when the endometrium specimen is taken before menstruation begins, whether the maximum secretory changes have or have not taken place. That is, the specimen may be taken with the expectation that menstruation will begin within the next twenty-four hours, and had the endometrium not been traumatized by the procedure, that particular period might not have begun until forty-eight or seventy-two hours later. As a consequence, had such been the case, a specimen is obtained which does not show the changes which would have been seen had the specimen been taken later.

In consideration of these factors, we have been doing endometrial biopsies after menstruation has begun. We have found that nearly all the specimens which were obtained within the first three hours are satisfactory for histologic examination, and all taken within the first two hours have been satisfactory. Specimens taken after three hours may be unsatisfactory, since disintegration and desquamation may have proceeded to a point where the cellular structures are destroyed.

The ideal time would be immediately after bleeding began, but this is not usually possible. One can always be certain, if the specimen is taken at this time, that all the changes have taken place which are going to take place.

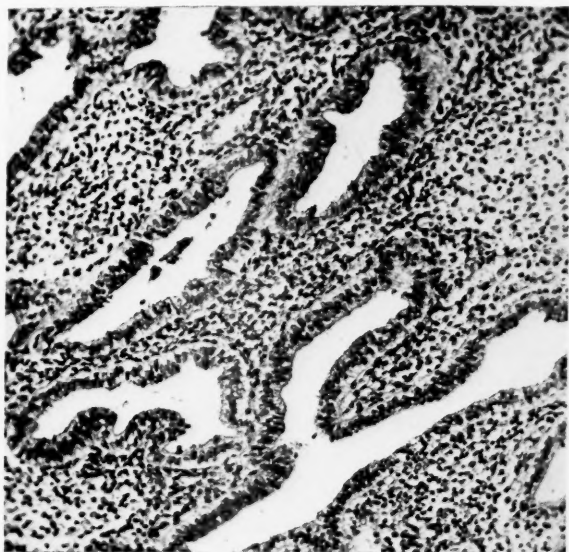


Fig. 1.—F. H., aged 18 years. Endocrine investigation in relation to epileptiform attacks. Patient was three days over her expected menstrual period, and was of the opinion that menstruation was imminent. Biopsy was done, but the period did not begin until four days later. Here is a specimen obviously deficient in the normal changes, but since the specimen was taken four days too soon, no conclusions can be drawn from it.

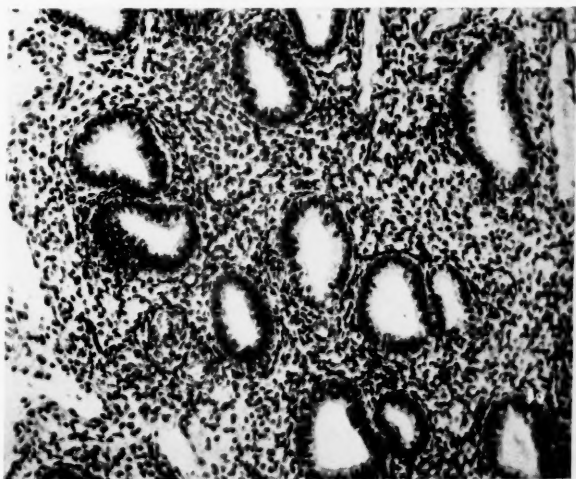


Fig. 2.—G. S., aged 37 years. Sterility study. This specimen is generally of the same pattern as shown in Fig. 1. However, it was taken within an hour after menstruation began. The cellular structure is intact. It shows a definite endocrine deficiency, particularly in that of progesterone. Since menstruation had already begun, the development is maximal, and the deficiency seen is actual.

Another important advantage of this method is that one does not inadvertently do an abortion, since one can never be certain that the next menstrual period will occur.² The only disadvantage is that it is not always feasible to obtain the specimen during this rather narrow range of time, and one must wait until the next period.

Biopsies done in the office on the menstruating uterus have not been followed by any undesirable consequences.

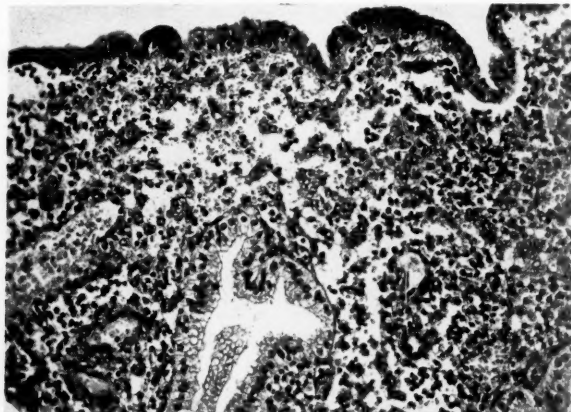


Fig. 3.—W., aged 25 years. Sterility study. Specimen taken about two hours after menstruation began. Changes shown are within normal limits, and the cellular structure is intact. The fact of ovulation and corpus luteum formation and activity is definite.

CONCLUSIONS

1. It is essential that endometrial specimens be taken as late in the menstrual interval as possible, to insure finding maximal endocrine changes.
2. Because of the variation in menstrual intervals, and because conception may have occurred following the preceding ovulation, it is advisable to secure the specimen after the onset of menstruation. This insures the maximal changes and permits more accurate diagnosis of endocrine factors, and obviates the chance of interrupting an early pregnancy.
3. Specimens obtained within two hours after the onset of menstruation are histologically intact.
4. There is no added risk in doing the biopsy at this time.

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THE COEXISTENCE OF CARCINOMA AND TUBERCULOSIS OF THE UTERUS

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THE simultaneous occurrence of tuberculosis and cancer in any organ is rare, and, in the uterus, is extremely rare. This fact alone, coupled with the interesting clinical and pathologic features that it presents, warrants a reporting of this case and a review of the literature.

CASE REPORT

Mrs. S. M., a Syrian-Jewish married woman of 46 years, was admitted to the Israel Zion Hospital on Feb. 24, 1938, with the chief complaint of vaginal bleeding. Family history and past history were irrelevant. She was gravida iv and para i. A son, aged 33 years, was in good health. The menstrual cycle was $14 \times 30 \times 6$, with menopause at the age of 40. For four weeks before admission she had a profuse painless vaginal bleeding. She lost 14 pounds in weight within one year. Physical findings were essentially negative. She was fairly well nourished. Heart and lungs were negative. Uterus was soft, boggy, and retroverted. Cervix was eroded. Blood examination showed erythrocytes 4,000,000, leucocytes 8,000 per c.mm. with a normal differential. A preoperative diagnosis of retroversion, cervical polyp, and fibroid uterus was made. On Feb. 25, 1938 a total hysterectomy was done, leaving both adnexa which appeared normal. When tension sutures were introduced in the uterus during the operation, pus escaped along the suture lines. This was interpreted as being due to pyometra. The postoperative course was uneventful, and patient was discharged twenty-two days later. When seen, twenty-two months after the operation, the patient was apparently in good health. She had gained 20 pounds in weight and, as far as could be determined, she had no symptoms or signs referable to the lungs or pelvic organs. A roentgenologic examination of her lungs was essentially negative. She has also been followed up at the Memorial Hospital of New York, where no treatment was given her, as "at no time was any lesion found after the operation."

Pathologic Findings.—Gross Appearance of Uterus: Uterus was rather small, weighing 60 Gm. and measuring 70 mm. in length, from 25 to 30 mm. in width, and from 20 to 30 mm. in thickness. The fundus was rounded, globular, and fluctuant. On the posterior aspect in the midline, 2 cm. distal to the fundic rim, a subserous, pea-sized, calcified yellowish nodule was seen. On inserting a fine probe within the cervical cavity, the latter was found to end blindly at the internal os and no continuity between it and the uterine cavity could be established, except by a forceful thrust of the probe. The cervical canal was narrow, but free from exudate. The cavity was filled with a thick, stringy yellowish white purulent matter. The entire endometrium from the fundus and to the internal os presented a ragged, cupped out, honeycombed appearance (Fig. 1). On closer inspection, numerous pin-point-sized, yellowish tubercles could be seen scattered throughout the endometrial surface. The myometrium was thin, averaging 15 mm. in width. The ulceration ceased abruptly at the internal os.

Cervix: Portio vaginalis was smooth, pinkish, and glistening. At its junction with the cervical canal, there was a small, fairly circumscribed nodule, 8 mm. in diameter, which was slightly raised and its upper surface somewhat roughened (Fig. 1). On section, it showed slight thickening of the lining epithelium.

Microscopic Findings.—Section of the cervix, in the region of the grossly observed nodule, showed the surface to be mostly ulcerated and only partly lined by considerably hyperplastic epithelium which passed abruptly into a diffusely growing tumor (Fig. 2). This consisted mainly of masses of polyhedral or spindle-

shaped cells arranged in solid, moderately branching plexiform epithelial masses. There was generalized nuclear hyperchromatism and a moderate number of mitotic division figures. The tumor was more or less limited in its spread and did not invade beyond the lower level of the cervical glands. At the lower zone of the proliferating tumor nests, a rich lymphocytic infiltration was seen. *Sections of uterus* (Fig. 3) showed the endometrium to be poorly outlined and replaced in many areas by a wide, ill-staining necrotic layer bordered by dense zones of lymphocytes. Epithelioids and giant cells of the typical Langhan's type also were found in considerable number. In the deeper layers of the myometrium the lymphocytic infiltration was more pronounced. The tuberculous process extended to the ostia of the resected tubes. Ziehl-Neelsen stain of the endometrium was negative.

Pathologic Diagnosis.—Epidermoid carcinoma of the cervix, Grade II. Chronic ulcerative caseous tuberculosis of the body of the uterus with pyometra, and miliary tuberculosis of the uterine serosa.



Fig. 1.—Uterus, laid open, showing extensive tuberculous ulceration of the entire endometrium, and the carcinoma of the cervix (the latter marked by arrow). ($\times 3$.)

DISCUSSION

Review of Literature and Frequency.—The co-existence of cancer and tuberculosis in the uterus is extremely rare. Strachan,¹ in a review of this subject, states that he found only 8 such cases reported in 1924, 7 from Germany, and 1 from France. He added one case of his own, which, according to his statement, is the first of its kind ever to be reported in the English literature. In our review of the literature, which appears to be more thorough, but perhaps also not all-inclusive nor exhaustive, we found altogether 27 such cases reported, not counting those which were merely cited in statistical tables or reviews (such as Lubarsch's and

Ferroni's). It would appear that the only case reported in the American literature is that of Gais.²

At this point, it should be mentioned that a rigid criterion is to be applied in accepting such cases, so that only those in which both carcinoma and tuberculosis were proved beyond doubt are to be included in this review. Thus, cases of a "carcinomatous degeneration of a fibroid"(!)³ and the like, which are cited in the literature as instances of association with tuberculosis of the endometrium, cannot, for obvious reasons, be accepted in this collected series.

No mention is made of such cases by Kaufman,⁴ although he states that "in rare cases the combination of cancer and tuberculosis is seen." Lubarsch,⁵ however, found 29 cases of cancer-tuberculosis combination in 129 cancers of the uterus, or 22.5 per cent. Imamura⁶ found 8 such combinations among 3,103 patients with carcinoma of uterus, or in 0.25 per cent of all cases of cancer of the uterus. Similar cases of combined tuberculosis and cancer have been described by a number of observers in other organs, such as in the central nervous system, gastrointestinal tract, breast, skin, lungs, kidney, urinary bladder, penis, face, lips, tongue, larynx, and other organs.



Fig. 2.



Fig. 3.

Fig. 2.—Low power photomicrograph of cervix ($\times 100$), showing an epidermoid carcinoma, Grade II, plexiform in structure, growth being limited to the lower level of the cervical glands.

Fig. 3.—Photomicrograph of uterus, showing extensive caseation-necrosis of most of the endometrium on the left, lymphocytic and epithelioid zones on the right and many Langhans' giant cells scattered throughout. Three normal glands are seen in the upper right ($\times 28$).

Tuberculosis of the female genital tract by itself is rather infrequent. According to King⁷ and Greenberg,⁸ pelvic tuberculosis occurs at the frequency of 1 to 8 per cent of all pelvic inflammations. In the tuberculous institutions, according to the statistics of Stopper and Posner,⁹ the incidence is 20 to 30 per cent. At the Israel Zion Hospital, a general hospital which is representative of a cross section of a metropolitan American community, tuberculosis of the female genital tract was encountered 8 times in 22,000 surgical specimens within ten years, giving it a percentage of 0.03 per cent, and only 2 times in the past four years in 2,000 operative gynecologic cases, an incidence of 0.1 per cent of all gynecologic conditions.

TABLE I. SCHEMATIC TABULATION OF REPORTED CASES IN THE LITERATURE OF COMBINED CARCINOMA AND TUBERCULOSIS OF THE UTERUS AND CERVIX

AUTHOR AND YEAR	AGE	SYMPTOMS AND SIGNS			PATHOLOGIC LESION				
		MENORRHAGIA	METORRHAGIA	PAIN	CARCINOMA OF CERVIX	CARCINOMA OF ENDOMETRIUM	TUBERCULOSIS OF CERVIX	TUBERCULOSIS OF ENDOMETRIUM	TUBERCULOSIS OF MYOMETRIUM
Von Franque 1st case (1894)	43	*	*	*		+		+	
Von Franque 2nd case (1894)		*	*	*	+		+		
Von Franque 3rd case (1894)	40	*	*	*	+			+	
Von Reeklinghausen (1896)		*	*	*	+	+		+	
Bass (1899)	61	*	*	*	+			+	
Wallart (1903)	55	*	*	*	+	+		+	
Wallart (1903)	50	*	*	*	+		+		
Wallart (1903)	37	*	*	*	+			+	
Stein (1903)	48	*	*	*	+			+	
Schottlander (1905)		*	*	*	+		+		
De Josselin DeJong (1906)	64	*	*	*		+		+	
Eisenstein (1910)	24	*	*	*	+			+	
O'Halluin and Delval (1910)	35	*	*	*		+	+	+	
Schmidt (1914)	55	*	*	*	+		+		
Strachan (1924)	40	*	*	*	+			+	
Gais (1926)	47	+	+	+		+			+
Menniti (1933)	50	*	*	*		+		+	
Menniti (1933)	46	*	*	+	+		+		
Kris (1933)	45	+	*	+		+		+	
Votta (1934)	53	*	+	+		+		+	
Soler (1934)	63	*	+	+		+		+	
Soler (1934)	40	+	*	*	+			+	
Tommaseil (1935)	37	++	*	*		+	+		
Schultze		*	*	*	+			+	
Monekeberg		*	*	*	squamous	adeno		+	
Ravid and Scharfman (1939)	50	+	+	*	+			+	

*Not mentioned.

Tuberculosis of the cervix is mostly a secondary infection. Altogether about 300 such cases have been reported in the literature,¹⁰ of which only 35 were found to be primary.

Carcinoma of the cervix occurs at a frequency of 90 per cent, that of the fundus 8 per cent, and of the endocervix 2 per cent of all uterine malignancies.

Clinical Picture.—There are no specific symptoms or signs characteristic of co-existent tuberculosis and cancer of the uterus. In fact, as seen from the review of the literature (Table I), in none of the cases were there any pathognomonic signs, the diagnosis having been made only during or after the operation by the surgeon or by the pathologist.

Certain signs and symptoms, however, when present, may be helpful in recognizing the coexistence of both of these lesions.

The most common complaint is menstrual irregularity, usually in the form of metrorrhagia. Pain appears to be almost constantly present, and is characterized usually as an aching sensation in the pelvic region, the back or in either lower quadrant, with occasional radiation to the thigh or vertebra. Occasionally, an

afternoon rise in temperature is noted. There may also be nervousness and irritability. It is to be emphasized, however, that the general systemic signs of tuberculosis are prominent by their absence. The patient is usually pale, sallow complexioned, and her anemia is not accountable for by the loss of blood through the menstrual disturbance, but could be attributed to the systemic tuberculosis infection. Pelvic examination usually reveals no suspicion of tuberculosis, and often is negative for malignancy as well. The entire physical examination is very often essentially negative.

PATHOGENESIS

Tuberculosis of the Female Genitalia.—This is mainly confined to the tubes and endometrium. Rarely, it may also involve the vulva, vagina, or the cervix.

It is the accepted view today that tuberculosis of female genitalia is mainly a secondary infection, with the primary focus being located elsewhere in the body, but chiefly in the lymph nodes or in the abdominal organs. The infection is usually a descending one, namely, from the tubes to the endometrium. This is borne out by the fact that, according to all statistics, the tube is involved in almost 100 per cent of the cases of pelvic tuberculosis, while the endometrium is affected only in 40 per cent. The mode of origin of tuberculosis of the cervix, when not associated with an obvious primary focus elsewhere, can be explained as being embolic in nature. For, as shown by the experimental work of Korper and Vidal,¹¹ it would appear that when tubercle bacilli gain entrance into the blood stream they disappear quickly from it and may lodge as emboli in various locations.

The infrequency of tuberculous involvement of the uterus, itself, as explained by some, is supposed to be due to the continuous cyclic physiologic activity of the endometrium with its periodic desquamation, which makes bacterial growth rather unfavorable. This, however, is rather doubtful, because no complete or even partial desquamation of the endometrium takes place in normal menstruation. Other factors, however, such as trauma, antecedent infection and other pathologic changes which interfere with the menstrual cycle, may, in some measure, favor the development of tuberculosis.

Tuberculous involvement of the endometrium may take place either via the blood stream, through a lymphatic spread from the tube, in association with tuberculosis of both tubes and ovaries, as a secondary spread from the lungs, bronchial or mesenteric lymph nodes, or, rarely, in generalized miliary tuberculosis. More rarely it may occur as an ascending infection via the lymphatics in cases of tuberculosis of the vagina or vulva.

It is noteworthy that, contrary to what may be expected, pulmonary tuberculosis, at least in its active form, is rather infrequently associated with pelvic tuberculosis. In only about 25 per cent of cases of pelvic tuberculosis were the lungs also involved.¹² But as in the majority of pulmonary tuberculosis, the hilar lymph nodes are also involved, these most likely form the source of uterine tuberculosis. Other lymph nodes, especially the mesenterics, are likewise a possible source of the infection.

ASSOCIATION OF CANCER AND TUBERCULOSIS

For the last one hundred years there has been waging a lively controversy as to whether tuberculosis and cancer can coexist in the same organ or not. Rokitsansky,¹³ in 1855, was the first to expound the view that there is a definite antagonism between the two, meaning that tuberculosis and cancer cannot be present in the same organ. However, under the influence of Votta's work,¹⁴ and through his own further experiences, he later changed his previous generally accepted view and admitted that carcinoma and tuberculosis can coexist, but that this occurrence was rather rare.

The coincidence of tuberculosis and carcinoma, as first suggested by Lubarsch in 1888,⁵ and widely quoted since, may be viewed as occurring in one of the following ways: (1) As a purely accidental occurrence, either disease having no influence one on the other. (2) Metastatic carcinoma may be found growing near an old tuberculous lesion or a fresh miliary tuberculous eruption, especially in a serosal spread. The cancerous cachexia, then, offers a good nutritional basis for

the dormant tubercle bacilli. (3) A fresh tuberculous infection becoming engrafted on a fully developed carcinoma. (4) Carcinoma is superimposed on a chronic progressive tuberculosis, which serves as a predisposing factor. (5) A hypothetical simultaneous occurrence of both cancerous and tuberculous processes.

Pettinari,¹⁵ in his work "The Antagonism of Malignant Tumors and Tuberculosis," came to the conclusion that there exists no local or general antagonism between the two. He found that there was no attenuation of the virulence of the tuberculous process in the presence of the tumor, nor were the invasive properties of the tumor in any way diminished when in direct contact with the tuberculous lesion. The latter, in fact, was replaced by the tumor. Others, like Aschoff,¹⁶ Wallart,¹⁷ Stein,¹⁸ and Von Franque,¹⁹ believe that in some cases tuberculosis even predisposes the growth of cancer. The problem of the so-called antagonism between tuberculosis and carcinoma formed the subject of a much heated controversy at the "Congress of the Italian League of Fight Against Cancer" in 1932, and found in Centanni its most fervent protagonist. However, no definite conclusions were arrived at in this Congress.

In experiments on animals, Ayellow,²⁰ in 1932, came to the conclusion that there is no antagonism between the two diseases. He also noticed that tuberculosis aggravates cancer, and in splenectomized animals there was an increase in the frequency of development of cancer as well as in the co-existence of cancer and tuberculosis. On the other hand, Centanni,²¹ in his experiments on mice, found that living tubercle bacilli inhibited the growth of implanted cancer.

As to the problematical question which comes first, it would seem, from perusal of the literature, as well as from our own case, that it is usually tuberculosis which precedes cancer. The tuberculous involvement of the endometrium in our case was of long duration, as evidenced by the extensive caseation which resulted in pyometra. On the other hand, the carcinomatous involvement of the cervix in this case was definitely of a relatively more recent occurrence.

PATHOLOGY

The gross and microscopic features vary according to the type and location of the tuberculous and cancerous lesions. Tuberculosis of the cervix may occur in either of the following forms: (1) Miliary, (2) ulcerative, (3) vegetative (papillomatous), or (4) hyperplastic.

The ulcerative form may be difficult to distinguish grossly from carcinoma. Tuberculosis of the uterus, as mentioned previously, is usually confined to the endometrium and is secondary to a lesion in the adnexa or pelvic peritoneum. It occurs mostly as a diffuse interstitial and ulcero-caseous form with pyometra. Rarely does it assume a disseminated miliary form. The infection, as a rule, is limited to the endometrium and in only a very small percentage of the cases it may spread through the myometrium and involve even the serosa. Occasionally, as seen in our case, calcified tuberculous foci may be found over the uterine serosa.

In the early stages of uterine tuberculosis, there may be extensive metaplasia of the glandular epithelium in the surface layer. Histologically, the typical tuberculous granulation tissue or discrete tubercle formation is the usual characteristic picture found. Diffuse necrosis and caseation may, however, also be seen. When the internal os is closed, as in our case, the uterine cavity becomes distended, fluctuant, may reach a considerable size, with secondary pressure atrophy of the wall, a typical pyometra.

Carcinoma of the uterus, in association with tuberculosis, may occur in any of the usual anatomic forms known. The gross and microscopic appearance of carcinoma of the cervix and fundus are well known today, and, as they form no special feature of this paper, will not be discussed here. Suffice it to say, that there are no fundamental differences in the gross and microscopic features of carcinoma of the cervix and uterus when occurring alone or when in association with tuberculosis.

DIAGNOSIS

The diagnosis of the coexistence of tuberculosis and cancer of the uterus, as pointed out before, is very difficult or well-nigh impossible. As a matter of fact, in none of the cases reported, not excluding our own case, was a preoperative

diagnosis made. This may be explained by the fact that the possibility of the association of the two conditions is not generally recognized, as well as because there are no pathognomonic signs that would lead one to suspect the coexistence of the two lesions. The patient usually presents herself for signs and symptoms relative to malignancy. If, however, at the same time she shows undue cachexia or debility, which is out of proportion with what is usually found in early uterine carcinoma, the possibility of the coexistence of tuberculosis should always be kept in mind. Diagnostic curettage performed in such a case should not rest with the finding of malignancy alone, but should also be supplemented by bacteriologic study of the curettings.

In the microscopic diagnosis of these two conditions two points must be kept in mind: (1) Occasionally atypically appearing epithelial hyperplasia may be seen in the neighborhood of a tuberculous focus, and (2) occasionally, as pointed out by Ribbert²² and Kermauner and Schottländer,²³ foreign body giant cells in the vicinity of a breaking down cancer may resemble and be mistaken for Langhan's giant cells. In tuberculosis, however, the typical histologic picture, and especially the finding of tubercle bacilli on smear or in the tissue, makes the diagnosis absolute. In the final differential diagnosis the rarer forms, such as nonspecific chronic endometritis and syphilitic endometritis, have also to be kept in mind. Animal inoculation and serologic studies will help in the final diagnosis.

SUMMARY AND CONCLUSIONS

1. A case of coexistent tuberculosis of the endometrium and carcinoma of the cervix is reported and a review of similar cases in the literature is given.

2. The pathogenesis and mode of spread of tuberculous infection of the female genital tract is discussed.

3. There are no authentic proofs to support the view of the existence of the so-called antagonism between tuberculosis and cancer in the same organ.

4. It would appear that tuberculosis usually precedes cancer when the two are associated in one organ. This association may be explained as a chance occurrence or by a predisposition of the tuberculous organ to the development of carcinoma.

5. No definite pathognomonic signs and symptoms exist for the association of the two lesions. However, undue anemia and debility, which are unaccountable by the usual metrorrhagia in cancer of the uterus or cervix, should be suggestive of the combined diagnosis of tuberculosis and carcinoma.

6. The therapeutic procedure to be adopted varies in accordance with the location and extent of each lesion and must be individualized for each case.

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AN APPRAISAL OF THE ROUTINE USE OF SPECIAL POST-PARTUM EXERCISE*

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WHAT is the value of the routine use of printed directions given to patients, which detail the kangaroo walk, knee chest, and other postures and exercises commonly recommended to minimize posterior displacements of the uterus in the post-partum period? How many patients with a retroposed organ in the early ante-partum period will maintain such malposition during and after the puerperium? Is such a condition influenced by special exercises or postural treatments? If so, to what extent? Is the incidence of retrodisplacements greater among primiparous or multiparous patients?

My purpose in presenting this subject is to offer some additional information on these and other rather controversial problems relating to uterine displacements. I shall not speak of the pathologic importance, the sequelae, the etiology, or the correction of such disorders by surgical or mechanical supports.

The material for this presentation has been collected by a long painstaking study of more than two thousand ante- and post-partum records of my private patients.

In this discussion a uterus is considered as retrodisplaced, when its long axis deviates posteriorly to the axis of the plane of the inlet. I have not classified the various degrees of misplacement nor have I tabulated retroflexion alone or retroversion alone, or both concomitantly.

At the expense of being a bit elementary and for clarity's sake, I might add that all pelvic examinations were made directly after the bladder was emptied. Further it must be remembered that the uterus is a mobile organ with a normal range of movement of almost 120 degrees. My findings, therefore, are merely relative in character.

The 2,150 records were examined, 228 of which could not be included because of the lack of sufficient detail. In this study the records are divided into two groups according to whether they had or had not received the exercise sheet in the early post-partum period. This sheet has on one side these words:

INSTRUCTIONS FOR MRS.-----

Four days after your baby is born, you should begin to strengthen your muscles that have been so stretched while carrying and giving birth to your baby. Every morning and night lie flat on your back without a pillow with your hands

*Presented at the Northeastern New York Obstetrical Society, May 15, 1939, and at the Medical Society of the County of Rensselaer, October 10, 1939.

beside your hips. Then raise your hips off the bed, at the same time draw up on your rectum as though you were trying to hold a bowel movement. Then replace your hips on the bed. Repeat this up and down movement, gradually increasing the number of times each day from five to forty, if possible.

These exercises will help you to regain your natural form, whereas inactivity with tight binders restricts movements and tends to keep the muscles soft and flabby. From the fifth day until four weeks after the baby's birth, you should not lie on your back any more than is absolutely necessary. This will help to prevent backward misplacements of your womb. Resting on the abdomen awhile each day is desirable and when up and about, walking around on your hands and feet for five minutes each morning is very helpful to prevent misplacements, especially when followed by a rest in the knee chest position as illustrated on the reverse side of this sheet.

You should report to me any bright red vaginal discharge that lasts longer than two days after leaving the hospital. Also phone for an appointment any time after the final examination (marked at the end of this sheet) if any vaginal discharge or other female trouble appears between your regular menstrual periods.

It is inadvisable for you to walk up and down stairs before the third week and only once a day during the third week after the birth. Your regular household duties must not be resumed until after the date listed below.

On the reverse side of the sheet, I have tried to picture to the patient the proper knee chest posture.

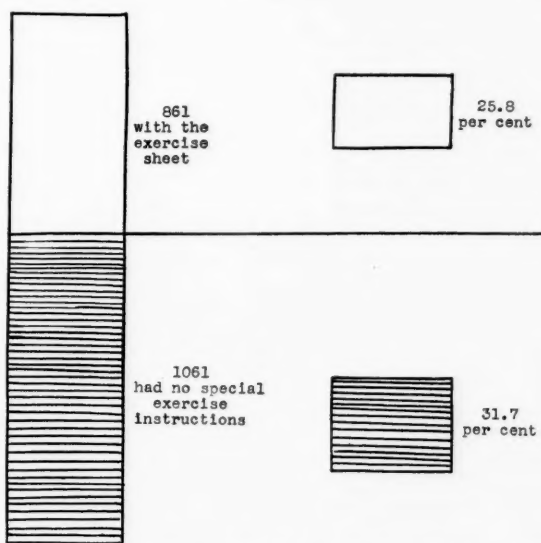


Fig. 1.—Showing post-partum deviations of the uterus in 1,922 patients, with and without exercise instructions.

MATERIAL OF THE STUDY

Fig. 1 shows 1,061 patients, illustrated by the shaded area, who had little other than occasional instructions, irregularly given by the nurse, to lie on the abdomen or to take the kangaroo walk. No printed or other illustrative detail was given to this group.

Of these, 31.7 per cent had retrodeviations at the sixth week's visit, whereas, there were 25.8 per cent posterior positions among the total of 861 patients who were given the exercise sheet. In other words, the tendency for displacements appears to be reduced 5.9 per cent among the exercise group.

Fig. 2 shows a study of 416 primiparous patients who had the results of a bimanual examination recorded before the end of the third month of pregnancy, as well as at the sixth-week post-partum visit. Two hundred and twenty-five patients were given the sheet and 191 were without it.

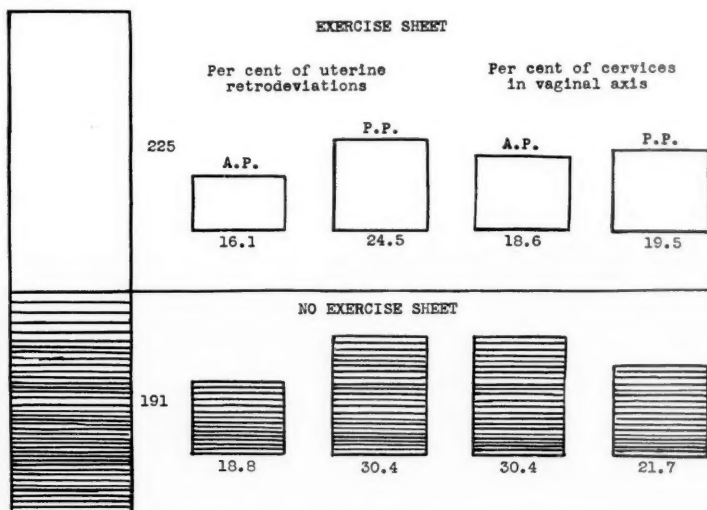


Fig. 2.—Showing results in 416 primiparous patients.

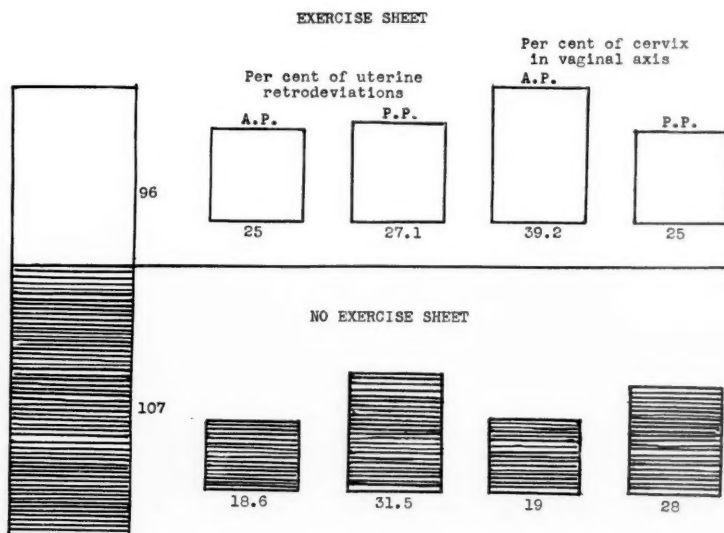


Fig. 3.—Showing results in 203 multiparous patients.

There are 16.1 per cent ante-partum uterine deviations in the exercise group and 18.8 per cent in the non-exercise group. At the sixth-week examination, this ratio stood at 24.5 per cent and 30.4 per cent, respectively. This tends to show two things: First, that there is an increase in the percentage of displacements in the post-partum over the ante-partum displacements in both groups. Second, that among the patients who did not receive the exercise sheet, 5.9 per cent more displacements occurred.

Fig. 2 shows the percentage of patients having the cervical canal in the vaginal axis. It is best studied with Fig. 3. It may be noted that in both primiparous and multiparous women, the incidence of cervixes in the vaginal axis, when compared with retroversions of the uterus, is higher in the ante-partum and lower in the post-partum group, or just the reverse of what happens to the uterus. I do not think that this has much bearing on our main subject but thought it worthy of observation as long as the data were available. It does show the unreliability of judging the position of the uterus merely by feeling of the direction of the cervical canal.

Fig. 3 presents similar statistical data on multiparous cases. Owing to the fact that such women are more prone to put off the time of coming to their doctor, and due to the lack of records showing the exact position of the uterus at the beginning of pregnancy, I found a total of only 203 records of this classification. Ninety-six patients were given the exercise sheet. They are represented by the clear upper portion. One hundred and seven had no exercise sheet. They are listed in the lower part of the oblong. Here we see that, regardless of less ante-partum retrodeviations among the patients who did not receive the sheet, nevertheless, those patients had 4.4 per cent more post-partum deviations of the uterus than those who were given the exercises.

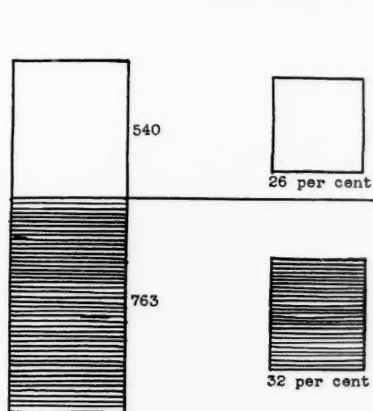


Fig. 4.

Fig. 4.—Showing post-partum findings in 1,303 patients in whom no ante-partum records were available. A 6 per cent decrease of retrodeviations occurs in the exercise group.



Fig. 5.

Fig. 5.—Showing normal increase of uterine displacements from ante to post partum in both groups (exercise and non-exercise).

The multiparous cervix shows the same tendency as the primiparous cervix; namely, in the ante-partum cases, a relatively greater number of cervixes are in the vaginal axis than there are deflected uteri. In the post-partum cases, on the other hand, there are fewer cervixes in the vaginal axis than there are uteri that are retrodeviated. This tendency is a variable consonate, and I do not think that much attention should be paid to it. It is possibly caused by stretching or tearing of an unusually short pubocervical fascia during labor.

Fig. 4 shows the record of 1,303 patients whose case histories contained no ante-partum pelvic findings, but the post-partum detail was complete. It will be noted in the shaded portion, that there are more in the non-exercise group than in the exercise group and that there were 6 per cent more retrouterine deviations in the non-exercise group.

Fig. 5 shows an incidental finding in this study which, I believe, has further bearing on our subject. There is a constant average increase of post-partum retrodeviations over the ante-partum deviations of the uterus, amounting to 8.7 per cent. This is 10 per cent among 416 primiparas and 7.5 per cent among 203 multiparas. As I have already pointed out, this increase is most marked among the non-exercise group.

Fig. 6 gives a summary of the value of special exercises among a total of 610 patients whose ante- and post-partum records were complete. In other words, they were examined sufficiently early in the ante-partum period to record the evident nonpregnant position of the uterus. Also a detailed record of their post-partum examination was available.

Here, too, the benefit of the exercise appears to be fixed at nearly the same figure as that obtained by the previous studies, namely, 7 per cent.

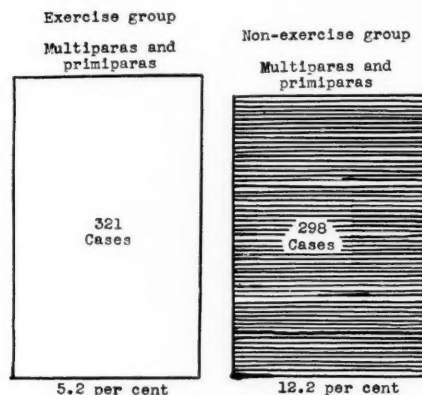


Fig. 6.—Showing comparative increase of uterine displacements from ante to post partum.

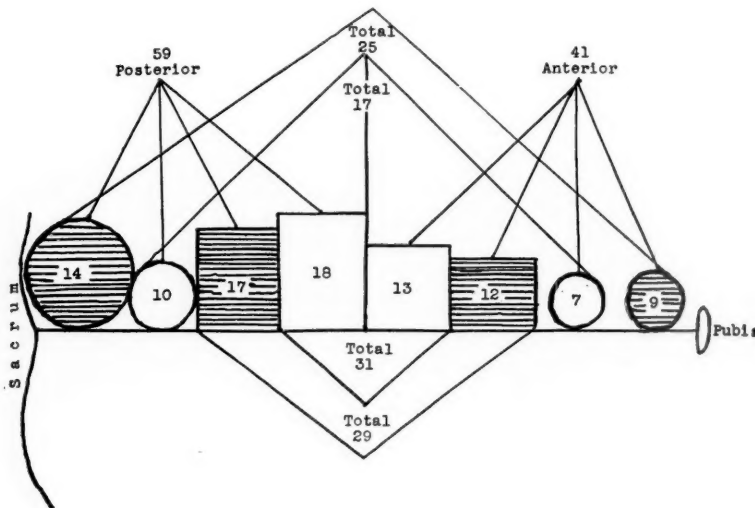


Fig. 7.—Showing post-partum findings in 100 cases of retrodeviations noted before the third month of pregnancy. Squares, primiparas; circles, multiparas; shaded area, no exercise; not shaded areas, with exercise.

Fig. 7 represents the records of 100 patients, all of whom were examined before the end of the third month of pregnancy and found to have a retrodeviation of the uterus.

Forty-one per cent of 100 known cases of ante-partum displacements are found to be normal positions at the six weeks' examination. Perhaps this is one of the factors that lead some women to say that they feel much better since having their baby. It may also be responsible for the abolition of some cases of dysmenorrhea.

It is my custom to make a routine pelvic examination of all nonmorbid puerperas on the seventh day. From this examination I am convinced that uterine involution is definitely enhanced among the patients who really do their exercises. I have noticed that leg strength comes back quicker in that group. It is possible that the routine use of such sheets minimizes the occurrence of embolism. I have not yet lost a patient from that cause.

Reports of this character, on the value of post-partum exercises, appear rather infrequently in the literature and show widely different conclusions. This may be due to personal interpretations as well as a disparity of accurate records.

Findley states that 20 per cent of the primipara and 25 per cent of the multipara-deviations are corrected by the knee chest and special exercise. Perhaps his patients are driven harder to their task than mine.

Schauffler, reporting on the use of the knee chest and special exercises in the puerperium of 169 patients, states that in the exercise group there were a total of 47.2 per cent misplacements, whereas in the non-exercise group there were only 34.5 per cent misplacements.

Lynch's excellent study of 1,230 cases showed 41.1 per cent of the entire series were displaced at some time during the first year following confinement. His figures show a wide discrepancy between private (19.6 per cent) and clinic (44.8 per cent) patients. I wonder if his patients were all examined by the same physician as was the case with these in this article.

SUMMARY

An analytical study of the uteri of 1,922 private obstetric patients is herein recorded; 861 were given special post-partum exercises. There were 1,061 controls. There was a decrease in the incidence of retro-deviations of the uterus, amounting to 5.9 per cent among the patients who were given the exercise sheet. This decrease varies but slightly among primiparas or multiparas. Of 100 known cases of retroverted uteri at the onset of pregnancy, 41 patients have been found normal at the sixth week post partum. The other 59 were still retrodeviated.

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2144 BURDETT AVENUE

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There exists a close anatomic and embryologic relationship between the reproductive and urinary tracts. The symptoms may be primarily due to one tract, or secondary to pathology of the other. Chronic cervicitis, prolapse, and pelvic tumors are often the exciting cause of urinary tract pathology. Pathology of the urethra or ureter may simulate gynecologic symptoms. Hence, complete urologic studies are indicated in doubtful cases or before major surgery. The two systems must be carefully considered in arriving at a diagnosis and the coordination of findings by the gynecologist and urologist will be most helpful.

J. P. GREENHILL.

THE ANAEROBIC STREPTOCOCCI IN TUBO-OVARIAN ABSCESS

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THE chronicity of tubo-ovarian abscesses is an old problem. In the 25 consecutive cases of this study, positive bacterial cultures were obtained from the pus in 23, contrary to the usually accepted idea that such pus is sterile. The anaerobic streptococcus was by far the most frequently encountered organism, being found in pure or mixed culture in 22 of the 23 positive cultures.

These 25 patients with chronic tubo-ovarian abscess were operated upon by the gynecological staff of the Henry Ford Hospital during the last half of the year 1937 and first half of the year 1938. Nineteen of the patients were white and 6 were colored. The average age of the group was 35.5 years, the oldest being 52 and the youngest 24. Seventeen were married, 3 single, 2 widowed, 1 separated, and 2 divorced.

The majority of the patients presented a history of recurrent attacks of lower abdominal pain and backache extending over a period of time varying from six months to fourteen years. The average duration was 25.3 months. The nature of the origin of these abscesses was obscure. Six of the patients gave definite history of previous gonorrhea and 6 admitted one or more previous abortions.

The average preoperative temperature was 99.2° F.; 10 had normal and 15 had elevations of temperature, the highest being 102° F. The white blood count was within normal limits in 8 cases and elevated in 17, the highest being 16,500.

All of the patients in this series were operated upon. In 22 cases the abscess was removed through an abdominal incision. Of the remaining three, two had a posterior colpotomy, and the other a posterior colpotomy followed by abdominal incision and drainage. Two of these patients died, one with symptoms of a terminal meningitis, and the other of acute postoperative peritonitis.

Specimens of the tubes and ovaries were examined in the department of pathology of the Henry Ford Hospital. In each instance a microscopic diagnosis confirmed the gross of chronic inflammation.

The pus obtained from the abscesses at the operating table was immediately inoculated (within five minutes) upon blood agar glucose slants and brain broth. Cultivation was done under aerobic, anaerobic, and partial (CO₂) tension for a period of at least ten days. One of the two negative cultures resulted when a period of time of two and one-half hours elapsed between operation and implantation of the pus on artificial media. Subcultures were made for study and identification of the various organisms.

The aerobic bacteriologic findings in the 25 patients appear in Table I and the anaerobic in Table II.

Some form of the streptococcus was isolated by anaerobic methods in 22 of the 25 cases. The majority were obligate anaerobes, but 7 species, after subcultivation,

TABLE I. SHOWING INCIDENCE OF AEROBIC BACTERIA

ORGANISM	NO. OF CASES
1. Nonhemolytic streptococcus	3
2. <i>B. coli</i>	2
3. Staphylococci	2
4. <i>B. pseudodiphtheriae</i>	2
5. Hemolytic streptococcus	1
6. Gonococcus	1
7. Negative cultures	17

TABLE II. SHOWING INCIDENCE OF ANAEROBIC BACTERIA

ORGANISM	NO. OF CASES
1. Streptococci	22
2. <i>B. melanogenicum</i>	5
3. <i>B. pseudodiphtheriae</i>	4
4. Yeastlike forms	2
5. Unidentified gram-negative bacillus	1
6. Gram-positive streptobacillus	1
7. Negative cultures	2

could be grown under partial (CO_2) tension or aerobic conditions. The latter therefore would seem to fit into that group of streptococci designated as "microaerophilic" by Meleney.¹ Two strains of these anaerobic streptococci were definitely hemolytic, one green producing, and all others nonhemolytic. They were all gram-positive after subcultivation, occurring in diploforms and short chains. Morphologically they seemed to fall into two subgroups, A and B; similar to groups A and B of Colebrook and Hare;² Group A being cocci of approximately the usual size of the common aerobic streptococcus, and Group B being micrococci extremely difficult to keep alive (see Table III). The organisms in Group A could be further classified by their ability or inability to produce putrid products during their growth. Those producing a putrid odor were apparently similar to the anaerobic *Streptococcus putridus* (later *putrificus*) described by Schottmüller³ and later by Schwarz and Dieckmann,⁴ and Schwarz and Brown.⁵ Sugar fermentation studies did not permit further classification of these cocci. Taylor⁶ stated that sugar fermentation tests were not likely to aid in their classification.

TABLE III. CLASSIFICATION OF ANAEROBIC STREPTOCOCCI ISOLATED IN THIS SERIES

Group A:
gr +, short chained coccus with many diploforms of approximately the same size as the common aerobic streptococcus; obligate anaerobes; nonhemolytic.
I. Those capable of producing putrid products.
II. Those incapable of producing putrid products.
Group B:
gr + micrococci occurring in short chains and clumps; very slow growing and difficult to keep alive; obligate anaerobes; non-hemolytic.
Group C:
gr + hemolytic, obligate anaerobic coccus of approximately the same size as the common aerobic streptococcus.
Group D:
gr + coccus, similar in size to those in Groups A and C; isolated by anaerobic methods and later grown aerobically or under partial (CO_2) tension.

In ten instances an anaerobic streptococcus was the only organism recovered; in 7 cases it was associated with one other bacterium, in 2 cases it was found with 2 other bacteria, in 1 case with 3 other bacteria, and in 2 cases with 4 others.

The pathogenicity of these streptococci for laboratory animals was very low. Intraperitoneal injections in rabbits and guinea pigs did not produce fatal peritonitis. Small subcutaneous abscesses were produced in guinea pigs by 2 of the strains, while small areas of induration or no demonstrable lesions were produced by the remainder.

DISCUSSION

The pus of chronic tubo-ovarian abscess has been reported to be bacteriologically sterile in the majority of cases as is shown in the collected series of cases in Table IV. The explanations that are given

for this high incidence of negative cultures are: (1) that the bacteria contained within the abscess lose their virulence and die because of a deficiency of oxygen and poor nutrition, and (2) the active acquired immunity of the body kills the bacteria.

The source of the anaerobic organisms which were found in the pus of tubo-ovarian abscesses in our series would seem to be the lower genital tract, namely the vagina and cervix uteri.

Anaerobic streptococci have been repeatedly cultured from the vaginal tract by Krönig⁷ (1895), Menge⁸ (1895), Halle¹² (1898), Williams,⁹ Schottmüller¹⁰ (1911), Rosowsky¹¹ (1912), Schweitzer¹⁶ (1919), Schmidt⁶ (1919), Soule and Brown¹² (1932), and Carter and Jones¹³ (1937) and others. Burt-White and Armstrong¹⁴ cultured anaerobic streptococci from 35.9 per cent of 153 cervices.

Anaerobic streptococci had been isolated in 1897 and 1899 by Krönig and Menge from parametrial suppurations in infected puerperal cases. Schottmüller (1910) found the anaerobic *Streptococcus putridus* (later *putrificus*) in the pus of parametrial suppuration, purulent salpingitis, and pelvic abscesses, principally following septic abortions or puerperal cases. He raised the question whether the salpingitis in the observed cases was primarily caused by the *Streptococcus putrificus* or whether the latter was present as a secondary invader following primary gonococcal infection. He concluded that the anaerobic streptococcus could primarily cause salpingitis in spite of his invariable failure to produce experimental lesions with the strains he isolated.

Curtis¹⁵ (1921) described anaerobic streptococci in five cases of adnexal or parametrial suppuration.

The high incidence of positive cultures in our series may be explained by: (1) the fact that anaerobic cultures were made on suitable media immediately after the pus was obtained at operation, and (2) the fact that these cultures were held under observation for a period of seven to twenty-eight days. Comparing Tables I and II a striking difference is noted between the number of negative aerobic cultures (70 per cent) and the number of negative anaerobic cultures (6 per cent). This emphasizes the importance of making prompt routine anaerobic as well as aerobic cultures.

Several hypotheses may be advanced to explain the presence of anaerobic organisms in these abscesses: (1) Bacteria present in the vaginal secretion may accompany the gonococcus in its ascent to the tube and may persist after the latter dies; (2) they may have the same mechanism of ascent as the gonococcus, and alone may be capable of setting up a state of prolonged inflammation and suppuration; (3) the abscesses may become secondarily infected from a neighboring adherent viscus such as the intestine. Satisfactory proof for any of these hypotheses is lacking.

It is difficult to explain a prolonged state of tubo-ovarian suppuration in the absence of viable microorganisms. Contributory evidence of the presence of such viable microorganisms may be found in three observations: The putrid odor of the pus in many instances, the occasional occurrence of deep wound abscesses after operation in the face of a negative aerobic culture of the tubo-ovarian abscess pus, and the development of a fatal peritonitis after salpingo-oophorectomy for

TABLE IV. COLLECTED SERIES OF CULTURES OF PYOSALPINX AND TUBO-OVARIAN ABSCESS*

AUTHOR	NO. STERILE	GONOCOCCI	STAPHYLO- COCCI OR STREPTO- COCCI	TOTAL NO. OF CASES
1. Charrier	6	9		15
2. Hartman and Morox	13	13	4	33
3. Kelly	33	8	1	43
4. Legros	1			1
5. Martin	63	21	7	109
6. Menge	68	22	5	106
7. Orthmann	7	1		8
8. Prochnownik	5	1	21	27
9. Reichel		1		1
10. Schaffer	10			11
11. Schuta	69	23	15	109
12. Schmidt		1		1
13. Steman		1		1
14. Wertheim	72			116
15. Westermarck		1		1
16. Whiteside	9	7	3	27
17. Witte	15	7	4	39
18. Zweifel	32	8	3	44
19. Rist	3	2	1	7
20. Macheyrodt			1	1
21. Durk			1	1
22. Bellei	5	1	12	20
23. Walsh	9	7	5	25
24. Trommel			1	1
25. Andrews	26	5	2	42
26. Cosma	11			11
27. Joyle	35			39
28. Wiener			1	1
29. Noeggerath and Wertheim	122	56	17	312
30. Rosenow and Davis		1	2	3
31. Studdiford, Casper and Seodron	8	16		24
Totals	632 (53.6%)	212 (18.0%)	105 (8.9%)	1179

*NOTE: Bacteria, other than gonococci, staphylococci, and streptococci, were not tabulated but were included in the total number of cases.

chronic tubo-ovarian abscess. In our series of 25 cases the pus had a foul odor in 10 instances. Cultivation of the anaerobes recovered produced a similar odor. The anaerobes which we believe were responsible for this foul odor were forms of the anaerobic streptococcus and the black-pigment-producing *B. melanogenicum*.¹⁶

The pathogenic power of anaerobic streptococci for man is difficult to determine. The great majority of investigators have found these bacteria to have little or no virulence for laboratory animals, with a few exceptions.

Wegelius¹⁷ noted small intraperitoneal abscesses in mice after their injection. Marwedel and Wehrsig⁶ produced an overwhelming infection in a guinea pig with a strain isolated from a war wound. Prevot⁶ demonstrated pathogenic effects such as local abscesses, edema, or occasionally death with his strains. Harris and Brown¹⁸ stated that three of their 57 puerperal fever strains killed mice in twenty-four hours. Colebrook and Hare² found that small subcutaneous abscesses were produced by 2 of their 7 strains recovered from puerperal sepsis.

There is some evidence that these bacteria, while usually existing as saprophytes in the mucous cavities of man, under favorable conditions may assume virulence. Notwithstanding the low virulence for laboratory animals, the frequent presence of anaerobic streptococci, often in pure culture in inflammatory states, such as puerperal sepsis, chronic bartholinitis, appendicitis, peritonitis, pyelitis, pulmonary abscess, putrid empyema, endocarditis, and suppurative otitis media, strongly suggests their pathogenic nature for man.

SUMMARY AND CONCLUSIONS

1. The bacterial content of 25 consecutive cases of chronic tubo-ovarian abscess was studied.
2. The anaerobic streptococcus alone or associated with various other microorganisms was demonstrated in 22 of the 25 cases.
3. Negative cultures were found in only 2 of the 25 cases.
4. A series of cultures of tubo-ovarian abscess and pyosalpinx were collected from the literature.
5. The value of routine anaerobic as well as aerobic cultures is emphasized.
6. The importance of immediate cultivation and long incubation is stressed.
7. The pathogenicity of these anaerobic streptococci for man is suggestive, but has not been proved.
8. The presence of microorganisms growing in the pus of chronic tubo-ovarian abscess would seem to explain the characteristic recurrent attacks better than the assumption that the abscess becomes repeatedly reinfected from without.

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BLOOD PHOSPHATASE IN PREGNANCY AN INDICATION OF TWINS

A PRELIMINARY REPORT

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DURING the course of a nutritional study of pregnant women attending the Prenatal Clinic of the Toronto General Hospital, estimations of the plasma phosphatase* have been made by the method of King and Armstrong,† with modifications for the Evelyn colorimeter. The results of these determinations have shown that between five months and six months in pregnancy the phosphatase averages 6.4 units in 100 patients, few readings being below 4 units or above 9 units.

The possibility of a twin pregnancy was suggested when a reading of 14.6 was obtained in a patient three months before term. At this time, physical examination had not suggested twins. However, subsequent x-ray proved their presence.

Table I gives the findings in six twin pregnancies and those single pregnancies with abnormal or interesting phosphatase values.

Twins were suggested or confirmed in six cases by phosphatase readings more than double the average during pregnancy. Single pregnancies were suggested in three cases by normal phosphatase readings, where clinical examination and family history suggested twins. In one patient (B. McD.), unusually high phosphatase values were found throughout the last four months of the pregnancy. X-ray and finally delivery at term revealed the presence of a single normal fetus. The only abnormality found was moderate anemia throughout pregnancy. Other estimations upon the blood were as follows: Nonprotein nitrogen, 30 mg. per cent; calcium, 9.9; phosphorus, 5.0 mg. per cent. In this case there was no clinical evidence of biliary obstruction or liver disease.

*Phosphatase is an enzyme which is found where calcareous deposit normally takes place. It hydrolyses phosphoric acid ester and sets free inorganic phosphate. Growing bone has a high phosphatase activity, while cartilage has none. The formation of bone depends upon the concentration of calcium and phosphate, and also upon the hydrogen ion concentration of the tissue fluids. This enzyme is also found in the kidneys, blood, intestinal wall and liver.

The normal adult range (King and Armstrong) is between 3.7 and 13.1 units, the majority being between 5 and 10 units. Serum phosphatase has been found elevated in diseases characterized by marked osseous changes, such as osteoporosis, osteomalacia, Paget's disease, marked parathyroid hyperfunction, and local bone atrophy. It is also elevated in diseases of the liver, such as biliary obstruction, hepatitis, and cirrhosis of the liver.

†King, E. J., and Armstrong, A. R.: *Canad. M. A. J.* 31: 376, 1934.

TABLE I

	5-6 MONTHS UNITS	7-8 MONTHS UNITS	AT TERM UNITS		REMARKS
Average	6.45	11.74	16.82		Average of 100 pregnant women
T. J.	14.6	32.0	38.5	Twins	Suggested at 5½ months by high phosphatase. Proved by x-ray.
G. B.	11.0	15.7	22.0	Twins	Suggested at 6½ months by high phosphatase. Proved by x-ray.
M. D.	13.5	18.0	16.4	Twins	Twins suspected clinically as well as suggested by the high phosphatase.
E. H.	15.7	28.5	45.0	Twins	Suggested at 6 months by high phosphatase.
B. W.	-	22.8	29.5	Twins	Clinical and x-ray diagnosis at 8 months.
A. W.	-	22.0	25.8	Twins	Clinical and x-ray diagnosis at 8 months.
B. McD.	28.8	86.0	78.0	Single	Multiple pregnancy suggested by high phosphatase; x-ray negative; mother very anemic.
M. D.	-	13.0	-	Single	Miscarriage at 7 months. Petrified 4 months' fetus.
M. C.	-	8.5	-	Single	Clinical diagnosis possible twins; phosphatase suggested single pregnancy.
H. B.	4.5	-	-	Single	Family history of twins; phosphatase suggested single pregnancy. Miscarried at 7 months.
J. S.	4.0	-	-	Single	Clinical and family history suggested twins; phosphatase suggested single pregnancy.
S. H.	3.8	4.9	10.0	Single	Anencephalic infant stillborn. Low phosphatase led to the suggestion on the history of fetal anomaly.
B. T.	5.8	4.9	9.0	Single	Large spina bifida, Mongolian idiot.

SUMMARY

Early findings in a study of the phosphatase of the blood in pregnant women suggest the possible value of this test in the diagnosis of twins.

Notes, B.: Routine Treatment of Gonorrhea in Females—Nonantiseptic Method.
Med. Ann. Dist. Columbia 8: 111, 1939.

In August, 1933, treatment of gonorrhea in women was begun by creating a local reaction and drainage with the omission of antiseptics: (1) All cervixes with functioning cervical glands were cauterized one or more times with the electrocautery at intervals of two or more months in order to cause local reaction and to elicit better drainage of the active focus. (2) The urethral meatus and cervix were treated weekly with applicators saturated with 25 per cent silver nitrate in order to cause local reaction and to favor better drainage. (3) Douches of 1.5 per cent acetic acid (vinegar or physiologic) were taken by the patient at home twice daily with a fountain syringe until the cervix was healed and with a pressure syringe (bulb type) after the cervix was healed. Of 3,394 women with gonorrhea admitted as new cases to the gynecologic section of the Social Hygiene Clinic of the District of Columbia 705 were discharged as cured by the foregoing method. The author concludes that antiseptics should be abandoned in the treatment of gonorrhea in women and that every patient who cooperates can be cured.

J. P. GREENHILL.

ANURIA FOLLOWING BLOOD TRANSFUSION

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FOREIGN literature repeatedly describes certain reactions which occur after nearly every major transfusion. Besides albuminuria and hemoglobinuria,² a grave or even fatal renal complication may follow in the form of diminution up to complete suppression of the urinary flow.^{1, 3-5}

These grave transfusion dangers are charged to the reaction between the donor's erythrocytes and the recipient's plasma. The mechanical effect of these group reactions, agglutination and hemolysis, is connected with a more or less complete embolic blockade of the capillary circulation, especially in the kidney.^{6, 7}

The mutual reaction of different blood types manifests itself in the first place as agglutination, and second may be followed by a hemolytic phase. According to this interpretation, the two phenomena are closely interrelated; they appear as the components of an identical reaction, and the hemolysis is always preceded by agglutination. The "disagreement" of two blood types is the expression of a reaction between the agglutinin-agglutinin complex of the mixture (Dyke).^{6, 7}

I would like to report a personal case wherein anuria followed a citrate transfusion, only 60 c.c. of blood being administered.

A multipara, aged 30 years, was brought into the hospital in shock following incomplete, accidental miscarriage, large amount of blood being lost. Under anesthesia uterine cavity was packed. Nothing further was done and patient returned to bed. Blood count on entry showed 63.8 per cent hemoglobin with 3,590,000 red blood count. White count 23,750 with 93 per cent neutrophils and 7 per cent lymphocytes.

Within twenty-four hours the patient's hemoglobin was 44.6 per cent, red cells 2,580,000. In view of this it was decided to give the patient a citrate transfusion. A donor was selected, and by laboratory tests the patient's serum and donor's cells showed no agglutination, and patient's cells and donor's serum showed no agglutination. Blood Wassermann was negative.

Transfusion was started, and after administering only about 60 c.c. of blood, the patient complained of severe pain in her back, difficulty in breathing; pulse rate was 160 and patient appeared in extremis. Transfusion was immediately stopped and adrenalin was administered. Patient vomited considerable yellow fluid. She was treated for shock, and it was about one and one-half hours before she responded. She was not bleeding through pack, so vaginal packing was removed, following which large pieces of placental tissue were passed spontaneously.

Patient was given glucose intravenously 1,000 c.c. of a 10 per cent solution. Prior to her transfusion, patient had voided spontaneously, passing various quantities of urine, in fairly good sized amounts. The urine analysis on entry was essentially normal. Following the transfusion, and the severe reaction which the patient experienced, the urinalysis showed a two-plus albumin, hyaline and fine granular casts and a specific gravity of 1.007. There were no red blood cells present, but the field was loaded with white blood cells. Patient was catheterized and 980 c.c. of urine were obtained. Twenty-two hours after transfusion patient passed only 120 c.c. of urine despite fluid intake of 1,500 c.c.

It was noted that there was a gradual diminution of urine for the next forty-eight hours, varying from 250 c.c. to complete suppression. However, the patient's temperature and pulse appeared normal. She had no complaints with the exception that she could not urinate, and despite the administering of hypertonic glucose intravenously in small quantities, and giving salt solution by hypodermoclysis, only 30 to 40 c.c. of urine could be obtained by catheter in twenty-four-hour output.

Three days following this severe reaction, the patient's hemoglobin was down to 38.4 per cent, R.B.C. 1,840,000. Condition was naturally alarming, in view of the fact that the kidneys were not functioning, and the hemoglobin was very low. Another donor was selected, and another citrate transfusion attempted, and carried out successfully, patient receiving 500 c.c. of citrated blood without undue reaction.

All known means to stimulate kidney function were attempted, including calcium chloride intravenously, diathermy over kidney regions, and 50 per cent sucrose solution intravenously in quantities of 50 to 100 c.c.

Dr. Frank Hinman was called in consultation on the fifth postoperative day, and he suggested giving Fisher's solution, 1,000 c.c., intravenously twice a day. The bladder was irrigated with a 4 per cent boric solution, and following the first twenty-four hours of Fisher's solution, intake by mouth was 2,520 c.c. and output by catheter was 90 c.c. Small doses of Epsom salt were given by mouth and about the seventh day patient was quite edematous. However, fluid intake was kept up to 1,500 c.c. for twenty-four hours. Patient was not able to take very much by mouth because of nausea. Output gradually increased to 120 c.c. for twenty-four hours, and 255 c.c. and then finally on the tenth day output had increased up to 645 c.c., and the patient's condition gradually improved, despite the fact back and legs were still very edematous, and she complained of weakness and great difficulty in breathing, with considerable pain in lower lumbar region still present. On the eleventh postoperative day patient voided over 5,000 c.c. of urine.

Patient was definitely on the mend until the fourteenth day, and for no reason whatsoever, the patient's pulse went to 166, she became very dyspneic, and the medical consultant made a diagnosis of paroxysmal nodal tachycardia, with suggestive evidence of myocardial damage. Quinidine was administered for this condition, also coramine in fairly large doses until pulse gradually came down to 128 and remained between 128 and 140 for the next ten days.

Patient was eventually discharged on the twenty-sixth day in a weakened condition, but considerably improved.

COMMENT

Although the blood donor and recipient were cross-typed and said to be entirely compatible, this patient developed a blood-transfusion reaction, confirming the idea that the agglutinin content of some donors' blood sera may be so surprisingly high, namely, 1:200 instead of the usual 1:3; that serious results may ensue unless high titer sera are used when cross-typing the blood before transfusion. Cross-matching between patient and donor was rechecked on two different occasions following this reaction and the blood was found compatible.

We do not know whether this patient's kidneys responded to the Fisher's solution, which was given intravenously over a period of three to four days, or whether it was a combination of the Fisher's solution plus other things used to stimulate kidney function. The fact remains the patient got well.

Blood chemistry was not done due to the economic factor involved.

It is now about six months since the patient left the hospital, and on examination on different occasions, we find her in good physical condition. Her last urinalysis was perfectly normal and her blood count showed an 84 per cent hemoglobin with 4,110,000 red blood cells.

A kidney function test was done, dye being injected intravenously with the following results:

First specimen 30 minutes after injection	40 per cent
Second specimen 60 minutes after injection	20 per cent
Third specimen 90 minutes after injection	10 per cent
Fourth specimen 120 minutes after injection	5 per cent
Total	75 per cent

Blood chemistry at this time showed a nonprotein nitrogen of 35 mg./100 c.c. blood.

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THE ORAL ADMINISTRATION OF STILBESTROL

(SECOND CONTRIBUTION)

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IN A previous communication¹ we presented our results, using a new synthetic estrogen, stilbestrol, in the treatment of syndromes presenting signs of estrogenic deficiency. Since the results obtained were as satisfactory with stilbestrol as were previously experienced with biologic estrogens administered hypodermically, we were prompted to continue our studies.

Our clinical experience with orally administered biologic estrogens has been unsatisfactory. However, the desirability of utilizing this mode of administration and our previous success with stilbestrol by the intramuscular route, led us to investigate the value of this drug given orally.

Our clinical material consists of 57 cases from the Hutchinson Memorial Clinic of Tulane University of Louisiana and the private practice of three of us (J. C. W., B. B. W., C. G. C.). In this group of 57 cases, there were 20 classed as having a physiologic menopausal syndrome (Group I), 29 had postoperative or postradiation menopausal syndromes (Group II), while 8 cases were classified as manifesting hypoestrinism (Group III).

GROUP I. PHYSIOLOGIC MENOPAUSAL SYNDROME

The physiologic menopausal syndrome group consisted of 20 patients ranging in age from 35 to 51 years. Their complaints included various combinations of the following symptoms: headache, dizziness, nervousness, hot flushes, depression, muscle and joint pain, frigidity, insomnia, irritability, and vaginitis.

Routinely our patients were given 1 mg. of stilbestrol three times a day, orally. This dosage was adequate for the control of symptoms in the majority of cases, and as improvement was noted, the dosage and frequency of administration were diminished. A few patients were adequately controlled with as little as 0.1 mg. per day. If improvement was not satisfactory, the dosage was increased to as much as 15 mg. a day.

Of the 20 patients in this group, 17 were clinically improved, 2 reported slight improvement, and 1 was unimproved.

GROUP II. ARTIFICIAL MENOPAUSE

This group of 29 patients complained of postoperative or postradiation menopausal syndrome. Various combinations of the symptoms enumerated in the previous group were manifested by these patients, but were usually more severe in character. The basic therapeutic regime of 1 mg. three times a day orally was instituted, and individualized subsequently when necessary. Of the 29 patients included in this group, varying in age from 25 to 54 years, 27 were improved, 1 was unimproved, and one failed to continue therapy.

GROUP III. HYPOESTRINISM

There were 8 patients ranging from 24 to 34 years of age, manifesting symptoms attributable to estrogenic insufficiency. Their symptoms included nervousness, dizziness, hot flushes, irritability, frigidity, headache, insomnia, and muscle and joint pains. In addition, there were one case each of dysmenorrhea, dyspareunia, and menstrual edema, and 2 patients reporting severe premenstrual breast pain. The administration of the drug was varied in accordance with the time of appearance and the severity of the symptoms. All of this group showed marked improvement.

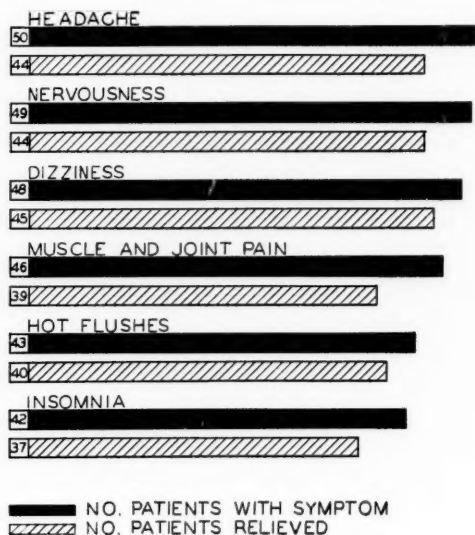


Fig. 1.

DISCUSSION

The frequency of nausea noted in our early experiences with oral administration of stilbestrol prompted us to seek to relieve this distressing symptom which often was the cause of rebellion on the part of the patient. At first we used soda bicarbonate, 4 Gm. given concomitantly and later, soda mint tablets. However, the results were not universally satisfactory. Upon the suggestion of a colleague,² working with oral administration of stilbestrol in children, we prescribed the tablets, powdered and mixed in a glass of milk. Nausea has been satisfactorily controlled in this manner, in the majority of the cases. No other untoward effects have been recorded in any case. In a few cases fullness of the breasts was present, but not to a distressing degree.

The results of oral administration of stilbestrol in the alleviation of individual symptoms is summarized in Fig. 1. Improvement is usually noted within a week. Many of the patients included in this series had been treated previously by stilbestrol hypodermically, and were then maintained satisfactorily by the oral route. Comparatively few patients had previous biologic estrogenic preparations, and the change to stilbestrol was more than satisfactory. Discontinuance of therapy occasions recurrence of symptoms within two weeks, necessitating re-institution of therapy. Withdrawal bleeding was noted in two patients who had long been amenorrheic.

No influence upon normal menstrual cycles was noted in this series.

Our observations in the oral administration of stilbestrol in cases of menopausal syndromes, physiologic and artificial, and hypoestrinism, lead us to recommend:

1. That therapy be individualized.
2. That the initial dosage be at least 1 mg. three times a day, and be varied as indicated.
3. When symptoms are improved that the amount be reduced to a satisfactory maintenance dose.
4. That the tablets be powdered and administered in milk.

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SPONTANEOUS OCCLUSIVE PYOMETRA

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PYOMETRA is of fairly uncommon occurrence and it is usually associated with cervical stenotic conditions, such as strictures resulting from childbirth, cervical operations, radiation, gonorrheal infection, and malignant infiltrations.

In women past the menopause, senile vaginitis is commonly encountered.¹ Shortly after the last menstrual period there begins a gradual atrophic development with the accompanying closure of the cervical canal and diminution of the size of the vaginal vault. These changes are the result of the failure of ovarian secretions which produce a terminal cicatricial closure of the cervical canal. With the occlusion of the canal, there is first a gradual retention of mucoid secretion followed by a contamination of this material. Nothing is noticed or complained of except possibly a sense of suprapubic fullness and pressure. When this pressure has become sufficient to overcome the pre-existing occlusion of the cervical canal, a gradual seepage of purulent material is noticed by the patient. Sometimes the escape of this retention is of sufficient quantity to afford spontaneous and complete relief for a short period of time. Operative interference alone seems to produce a cure.

Further mention should be made of the fact that females in the childbearing age have cervical strictures. A negative history of infection or instrumentation is obtained. Birth trauma can be ascribed as the cause with the usual sequence of retention followed by infection and either the appearance of a palpable suprapubic

mass or complaints of low abdominal pressure, pain, and cramps. A case of pyometra complicating pregnancy was reported by Gemmill.² In another instance an infected pregnancy in a 28-year-old female was suspected by Pride.³ At operation the cause was found to be a necrotic fibroid. A case of pyometra complicated by dermoid cyst twisted on its pedicle was reported by Godlewski.⁴

Malignant infiltrations of the cervical canal occur as in an endophytic type of cancer. The lumen is occluded with the resulting retention. There is a gradual foul discharge which leads to an investigation of its cause. Dilatation of the cervix is often found to be difficult, but immediate results and relief are obtained when the cervical canal is patent. Cancerous cells are found in the pathologic study. Reeb⁵ gives an account of a single case of pyometra, the genesis being a calcareous concretion in the neck of the uterus and obstructing it. Loranger⁶ calls attention to a case of noninfectious pyometritis produced by injections of large amounts of highly potent estrogenic substances.

CASE REPORT

M. G. S. (Unit No. 2135), aged 73 years, was admitted the first time to this hospital on Nov. 2, 1937 with a complaint of foul, bloody leucorrhea over a period of several weeks. The present illness was vague but was consistent in that the vaginal discharge was gradual in onset. Past and family histories were irrelevant.

Physical Examination.—Temperature 99.4° F., pulse 108, respirations 20, blood pressure 155/80. She was an elderly, poorly nourished woman. There was a partial denture and a marked pyorrhea. Neck revealed no adenopathy or abnormal pulsations. Examination of lungs revealed bronchovesicular breath sounds, no râles, or friction rubs. Percussion note was normal. Heart sounds were of fair quality. There were no murmurs. Breasts were flabby. Abdomen was below the thoracic plane and somewhat tender in the suprapubic and both adnexal regions. Normal peristaltic sounds were elicited on auscultation. Vaginal examination revealed an atrophic vaginitis, marital introitus, a very short, atrophic cervix, and a uterus that was twice normal size and tender on palpation. No palpable masses were present in either adnexal region. There was a moderate amount of foul, purulent discharge. The remainder of the physical examination was not remarkable.

Diagnosis.—Pyometra.

Laboratory examinations: Red blood count, 4,000,000; hemoglobin, 79 per cent; white blood count, 8,700; polymorphonuclears, 71 per cent; lymphocytes, 27 per cent; monocytes, 2 per cent. Wassermann and Kahn tests were negative. The urine was clear; specific gravity, 1.005; acid in reaction; sugar and albumin, negative; the sediment showed an occasional hyaline cast.

Two days after admission the patient was examined. The cervix was found to be atrophied, but the os was large and externally patent. A uterine sound was gently inserted and no apparent strictures were encountered. Approximately 3 to 4 ounces of purulent material exuded from the cervix. This was cultured and smeared. The culture showed mixed organisms, but the smear was positive for gram-negative intracellular diplococci. Following operation, the temperature rose to 100.4° F. for two days and then fell to normal. The patient gradually ceased passing any purulent material per vaginam and was discharged improved on the tenth hospital day. No other operative interference was believed justifiable because of her age. She was advised to return to the gynecologic out-patient clinic for follow-up. This she did twice and on both visits she still had a slight but persistent foul, purulent discharge. Her abdomen was negative on palpation. She then stopped coming to the out-patient clinic of her own accord.

On Nov. 8, 1939, patient again appeared in the out-patient clinic with the complaint of being unable to void except for a little dribbling. She was catheterized, but only 30 c.c. of urine was obtained. On vaginal examination a cystic mass 8 by 10 cm. was palpable. Admission to the hospital was advised with the provisional impression of pyometra.

She was admitted to this hospital with the complaint of not being able to void, a sensation of dull pressure in the pelvis, and a foul, purulent vaginal

discharge. These complaints dated back some three to four months previous to admission. Patient stated that during the night previous to admission she had saturated her nightgown and bedclothes by a profuse purulent discharge and estimated the amount to be a pint. Purulent discharge without blood had continued up to the present.

Physical Examination.—Temperature was 98.2° F.; pulse, 88; respiration, 24; blood pressure, 138/80. Patient was in no apparent distress. The examination was similar to the one two years previously except for definite tenderness in the suprapubic region and in both adnexa. There was a foul, purulent discharge per vaginam. Examination revealed a short, firm cervix; os was palpable just behind the cervix in the cul-de-sac. Exquisite tenderness was elicited on attempting to bring the fundus of uterus out of the cul-de-sac, and the attempt was unsuccessful.

Laboratory Examinations.—White blood count was 10,400; polymorphonuclears, 61 per cent; lymphocytes, 37 per cent; eosinophiles, 2 per cent. The urine was slightly cloudy, amber, acid in reaction, negative for sugar, but with a decided trace of albumin present. Smear of the discharge showed many pus cells, mixed bacteria, and a moderate number of extra- and intracellular gram-negative diplococci. The sedimentation rate was 23 mm. in one hour. Electrocardiogram revealed a sinus rhythm, ventricular rate 120, normal conducting mechanism.

The staff again was of the opinion that this patient had a pyometra. The patient was removed to the operating room and under nitrous oxide gas anesthesia a uterine sound was passed into the cervical os. The sound was introduced approximately three-quarters of an inch, at which time there escaped 6 ounces of pus. No obstruction was encountered. A smear and culture were taken. The uterine cavity was curetted with a dull curette. Patient was returned to the ward in good condition.

Pathologic Report.—(No. 17777.) Gross: Several bits of yellow slightly firm tissue. *Microscopic:* Small pieces of endometrium showing very few glands, all of which were benign. There was a heavy leucocytosis, some edema, and hemorrhage. Also a number of the stroma cells were swollen and had a pale-staining, foamy cytoplasm. *Diagnosis after gross and microscopic examination:* Infectious endometritis.

Smear reports showed many leucocytes, mixed bacteria, and a few extra- and intracellular gram-negative diplococci. Cultures revealed many mixed bacteria.

The patient was given a high calorie diet, vitamin and sulfanilamide therapy. A few days after admission the blood sulfanilamide level had reached 9 mg. per cent. The sedimentation rate changed to 31 mm. in one hour. No gram-negative diplococci were found in cervical smears at this time. Sulfanilamide was discontinued, and on the nineteenth hospital day the patient was discharged improved. At this time she was strongly advised to return to the out-patient clinic at regular intervals for follow-up observation and treatment.

Since discharge she has been to the clinic regularly. Cervical smears reveal an occasional gram-negative extra- and intracellular diplococcus. When last seen three months after her discharge from the hospital, the uterus was found to be in anterior position, mobile, of average size and unaccompanied by pain or tenderness. The cervical canal was patent without any further evidence of drainage and the smears were negative for the presence of gram-negative extra- and intracellular diplococci.

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PREGNANCY COMPLICATED BY FIBROMYOMAS OF THE LOWER UTERINE SEGMENT

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WHILE fibrotic conditions of the uterus are not uncommon in pregnant women, it is relatively rare to find large fibromyomas in the lower uterine segment of a pregnant uterus at or near term. The following is such a complicated case.

Mrs. G. H., para ii, gravida iv, was admitted to the hospital April 16, 1939.

Past History: In 1929 the first child was delivered spontaneously after labor was induced three weeks prematurely by the insertion of a bougie because of hypertension and marked edema. There were no headaches nor visual disturbances. The post-partum course was uneventful. In 1932 a dilatation and curettage was done to interrupt a one and one-half months' pregnancy because of pernicious vomiting which resulted in marked dehydration. In 1932 she had a spontaneous abortion at three months. In her childhood the patient had measles, chicken pox and scarlatina.

Family History: Her mother and father both died of cancer. A sister had a hysterectomy for uterine fibromyomas. Her menstrual periods began at 14 years of age, regular twenty-eight-day cycle, with four- to five-day duration of the periods. Last menstrual period, Aug. 17, 1938. Term date estimated as May 23, 1939. She gained 26¾ pounds in weight (128 pounds to 154¾ pounds). Her appetite was good and bowels were regular. She had marked nausea and vomiting during the first three months, requiring hypodermic medications for sedation. There was moderate leucorrhea but no history of bleeding or dysuria during pregnancy. She had experienced urinary frequency and nocturia prior to admission. For one month before admission, there was edema of the feet and ankles. For three days before admission the patient had severe headaches and slight nausea. There were no visual disturbances.

Physical Examination: The blood pressure was 178/106. The patient was a white, well-nourished female. Uterus was the size of an eight months' pregnancy. Fetal heart tones were 148, left upper quadrant. There was slight edema of feet and ankles. Otherwise the physical examination was negative. The heart was normal.

On April 16, 1939, the patient was admitted at 10:30 A.M., with a blood pressure of 192/112, pulse 92. One and one-half grains of nembutal were given. During this day the blood pressure ranged between 162/110 and 178/108.

Urinalysis: Specific gravity 1.015, reaction neutral, albumin heavy cloud, sugar 0, acetone 0, casts very rare hyaline and granular, leucocytes moderate amount, many epithelia. Hemoglobin was 80 per cent and red blood count 4,130,000.

On April 17, 1939, the blood pressure ranged between 174/110 and 144/96, and the urine showed heavy cloud of albumin every day with a few casts.

On April 21, 1939, the patient was examined vaginally, but it was impossible to identify the cervix or its external os. She was taken to the delivery room for a more complete examination, but still the cervix could not be found.

After April 23, 1939, the blood pressure ranged between 144/92 and 192/104. The urine continued a consistently heavy cloud of albumin with a few granular casts. She was having a salt-free diet and 1 ounce of magnesium sulphate every morning. The trend of the blood pressure and the results of the daily urinalysis did not indicate any improvement in the patient's condition.

On April 29, 1939 at 7:30 P.M. the patient began to have a slight bloody show and few cramplike pains.

On April 30, 1939, at 10:00 A.M. the patient was having pains every fifteen minutes with good contractions. The fetal head was floating above the inlet, and the fetal heart sounds were 148 on the left side of the abdomen above the navel. At 10:00 P.M. the blood pressure was 174/124. The baby's head was still high and the intern noted that there seemed to be some obstruction to the progress of the fetal head into the inlet. The uterus was oddly shaped. Some mechanical obstruction to the normal progress of labor seemed apparent, such as a cervical fibroid.

On May 1, 1939, at 12:02 A.M. the patient was taken to surgery and delivered of a living 5-pound 4-ounce female child by classical cesarean section. The uterus was closed after delivery of the child, and a panhysterectomy was performed. There was a large fibroid present on the posterior wall of the cervix which was 12 cm. in diameter. Another large fibroid was also present.

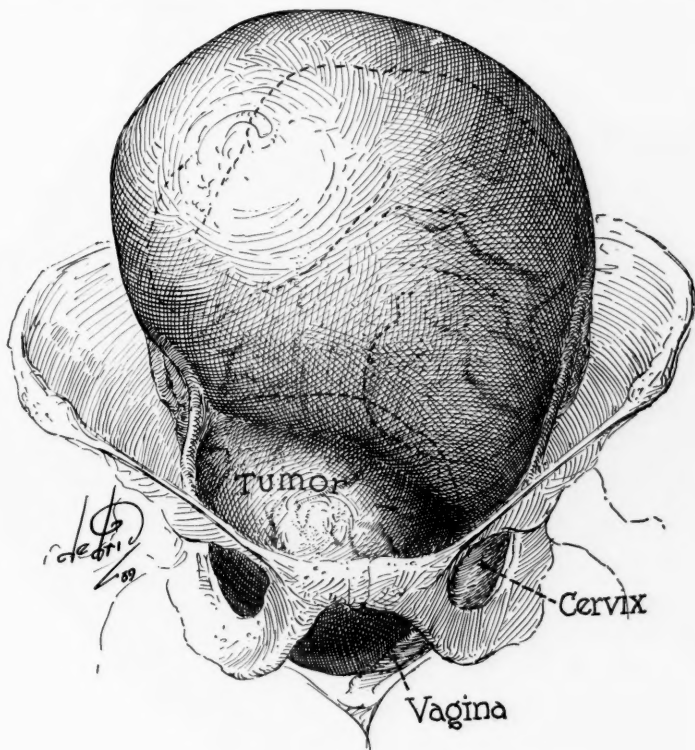


Fig. 1.

The blood pressure on return from the operating room was 164/130. The highest temperature postoperatively was 100° F. on the third day. The pulse during the day of the operation and through the fifth postoperative day ranged between 84 and 120.

On May 4, 1939, the third postoperative day, about 1:00 P.M., the patient became apprehensive and developed blurred vision. The blood pressure was elevated to 216/136 and the pulse was 120. One-fourth grain of morphine sulphate was given, followed by $\frac{1}{2}$ c.c. doses of *Tr. veratrum viride* at 3:15 P.M. At 4:45 P.M. the blood pressure was down to 94/62, and it reached its lowest level of 80/58 at 5:45 P.M. The pulse was 68. At 8:00 P.M. the patient complained of pain in the right hypochondrium. At 9:00 P.M. the blood pressure was 146/96, pulse, 92. On May 5, 1939, at 8:30 P.M., the patient again complained of pain in the right hypochondrium. This later moved to the right lumbar area. The patient was voiding

satisfactorily. Urinalysis showed heavy cloud of albumin, no casts, and otherwise negative.

On May 16, 1939, at about 5:00 P.M., the patient began to experience a very chilly feeling and the pulse became extremely rapid (160 at 7:00 P.M.). The temperature rose to 104.2° F. Thereafter the temperature gradually returned to normal. Systolic blood pressure remained around 130 and the urine still showed evidence of nephritis.

The patient was discharged on the twenty-fifth day. Her family doctor reports that with the exception of an occasional cloud of albumin in her urine, she is in good condition.

COMMENTS

Demonstrable tumors of the upper uterine segment are relatively more frequent during pregnancy than is generally supposed, but, as a rule, do not cause serious trouble during delivery.

Tumors of the lower uterine segment appear to be infrequent, but when present, during pregnancy at term, challenge the ingenuity and skill of the obstetrician. While it is well known that tumors of the lower uterine segment may be pulled up out of the pelvis into the abdomen by the upward traction of the fundus, this case demonstrates that occasionally this does not happen and obstruction to delivery is the result.

This patient seemed to have had none of the usual prenatal symptoms of fibroma complicating pregnancy, such as discomfort, pain, bleeding, and pressure symptoms, but was brought into the hospital and treated by her family physician, Dr. Wm. Jones, for a toxemia of pregnancy, which evidently from her history, was a toxemia of the nephritic type.

During the medical treatment of the toxemia, fibroids were not suspected, and it was not until the onset of labor that the intern and the family physician noticed the abnormal shape of the uterus during contractions, and consultation was sought. A definite hard mass had appeared above the symphysis which had pushed the head higher up and anterior. The fetal heart sounds remained rapid in the upper left quadrant.

At this time the cervix could not be located by vaginal examination but a hard mass could be felt higher up. Realizing that an obvious mechanical dystocia was present after the possibility of a twin pregnancy, an ovarian cyst or an overdistended bladder was ruled out, it was evident that we were dealing with a large fibroma or fibromas of the lower uterine segment and that during labor the lower uterine segment was partially pulled up and the uterus had rotated. This torsion or partial rotation of the uterus pulled the fibroids, which were posterior and lateral, into more of an anterior position, so that they could be felt above the symphysis.

A high classical cesarean section was immediately performed, after which it was discovered that the tumor mass could be dislodged and removed. This was done. Fig. 1 illustrates the size and extent of the fibroids and the impracticability of leaving the uterus.

The patient recovered after a stormy convalescence and returned home with a live baby.

MILLARD FILLMORE HOSPITAL

CARCINOMA OF THE CERVIX IN A SEVEN MONTHS OLD INFANT*

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(From the Margaret Hague Maternity Hospital)

CARCINOMA of the cervix is considered a malignant disease of adult life, generally occurring in a previously traumatized cervix. Therefore, its appearance at the age of seven months is startling and unusual, and difficult to interpret in terms of precipitating factors and carcinogenesis.

Cervical carcinoma in the early years of life is extremely rare. There is but one recorded case occurring in the first year of life, Bertkau's epidermoid carcinoma of the cervix and vagina in a seven-month-old child, confirmed by Robert Meyer. Meyer also confirmed Glockner's case of adenocarcinoma of the cervix in a seven-year-old child. Ganghofer's case of uterine carcinoma occurred at eight years and Bouner's at thirteen years.

The case herein reported is that of a baby in whom the symptoms of cervical cancer appeared at the age of seven months, was diagnosed positively by biopsy at nine months, and was followed through laparotomy, external and internal radiation, to autopsy fifteen months after the first symptom of cancer appeared.

Baby S. was born Feb. 21, 1937, normal spontaneous delivery at term, labor of twenty-seven hours, of a primiparous, 21-year-old, white female. Ante-partum course was normal; family history was negative for malignant disease. At birth the child showed no evidence of abnormality and weighed 3,190 Gm. (7 pounds). The neonatal period was normal. She was breast fed for eight months and then weaned.

On September 25, when seven months old, fresh blood was noted on a dry diaper, and on Oct. 1, 1937, blood was noted coming from the genitalia. This occurred again in November and on Dec. 1, 1937. When seen in December it was thought advisable to inspect the vagina, since the late onset of bleeding in infant life and the prolonged period of spotting seemed to rule out the physiologic bloody discharge occasionally seen neonatally. Through a Cameron nasal and aural speculum a polypoid growth about the size of a pea, purplish red and bleeding easily, was seen on the cervix.

A biopsy was taken and the pathologic report returned was adenocarcinoma of the cervix. This was noted to be highly undifferentiated.

The baby was admitted to hospital Jan. 10, 1938, for further examination, and was symptomless except for a brownish vaginal discharge. The weight was 9,450 Gm. (20 pounds 14 ounces). On January 15 another cervical biopsy was obtained and the same report was returned. This biopsy showed a great variety of nucleated cells, very numerous mitotic figures, and numerous blood vessels. Diagnosis: Carcinoma of the cervix.

The potential effects of radiation upon the child's development were considered. An operative attempt to conserve ovarian function was planned and performed Jan. 15, 1938. A low midline approach to the abdomen showed that the adnexa and uterus were normal. A small mass was palpated in the vagina in the region of the cervix with no signs of intra-abdominal metastases, indicating that the growth arose in the vaginal portion of the cervix. The left utero-ovarian ligament was divided, and the ovary carefully dissected with the mesovarium, avoiding the ovarian plexus at the hilum. This permitted the left ovary, attached only by the infundibulo-pelvic ligament with its blood supply, to be carried laterally two-thirds of the way from the pubes to the umbilicus, and there attached to the peritoneal aspect of the anterolateral abdominal wall. The postoperative course was uneventful.

*Presented at a meeting of the New York Obstetrical Society, January 9, 1940.

Radium therapy was begun six days postoperative, Jan. 21, 1938. The cervix was crossfired from five directions in 3,000 mc. doses; on January 21, to right and left groins; on January 22, to right and left trochanteric regions; and on January 23, to the lower sacral region, a total of 15,000 mc. hr. The transplanted ovary was carefully protected with adequate lead screens during the series of anterior treatments. There were two slight elevations of temperature during this period, to 101.6° and 100.4 F., for one day each, but no other systemic reactions. All vaginal discharge stopped one week from the date of the last treatment.

One week after the last treatment the vagina was inspected, using a Cameron nasal speculum. The cervix appeared normal, but there was a granulomatous-appearing area in the left fornix. Two weeks later biopsies were taken under direct vision, from the cervix and the left fornix. These both showed the changes of necrosis and chronic inflammation, but no evidence of malignancy.

During this stay in the hospital, from January 10 to February 27, the child appeared generally well. The discharge weight was 9,250 Gm. (20 pounds 6 ounces). The blood count on admission showed 87 per cent hemoglobin, 4.0 million red blood count; 18,000 white blood count with 65 per cent lymphocytes and 30 per cent neutrophils; one week following radiation it showed 80 per cent hemoglobin, 3.9 million red blood count, and 4,100 white blood count with 72 per cent polymorphonuclears and 22 per cent lymphocytes.

On March 14, 1938, the child returned, weighing 9,400 Gm. (20 pounds 12 ounces), which weight she maintained during the stay. April 1, 1938, the cervix was inspected and slight edema with telangiectases of the anterior lip was noted, together with cicatrization of the left fornix. At that time a small radium bomb was placed in the vagina, and a dose of 240 mc. hr. was given directly to the cervix. No immediate reaction was noted and the child was discharged on the next day.

During weekly observations in April and May she received four intramuscular injections of reticulogen in an effort to build up her red blood count. Her appetite was fair, vomiting was very occasional, and her weight remained at 23 pounds. May 26 the following note was made: "Vaginal examination with colposcope shows no recurrence or persistence of the cancer noted at previous examination. The cervix is clean, slightly irregular, and there is a large white scarred area to the left of the cervix on the vaginal vault. Another is also noted in the right upper vagina, and to a lesser extent there is scarred tissue in the mid third of the vagina. The scar is coursed with fine blood vessels and is obviously the result of radium burns. At no place is there the slightest evidence of abnormal tissue."

On August 1 a slight blood stain was seen on the vulva, the first vaginal bleeding noted since February 1. Speculum examination on August 4 showed a small papillomatous-like nodule on the posterior lip of the cervix. This was removed for biopsy and reported as recurrent carcinoma of the cervix (S. P. 3908).

On September 17 a special size vaginal radium bomb was applied and 509 mc. hr. given. Following this treatment an ulcerative proctitis and bladder irritation developed, subsiding in approximately one and one-half weeks. Blood count on this admission was 4,810,000 red blood count and 82 per cent hemoglobin.

On September 23 vaginal speculum examination revealed no evidence of carcinomatous tissue. The vaginal vault was the site of an extensive white scarred area with new blood vessels running through the area of the radium scar. The nodule in the vault, found on August 4 previous to radiation, had completely disappeared, and the patient was discharged to return for a check-up in two months.

In November the child had tonsillitis, became asthenic, lost weight, and was occasionally constipated. Vaginal speculum examination November 23 was negative, but a rectal examination revealed a mass about the size of a lime in the cul-de-sac. A diagnosis of metastatic carcinoma was made and she was re-hospitalized.

On the fifth and last admission, Nov. 28, 1938, the child was twenty-one months old. The blood count at this time showed 4,380,000 red blood cells and 75 per cent hemoglobin. The course from this point was progressively downhill. She had a foul-smelling, thick, mucoid, vaginal discharge on admission and soon developed

excoriation of the perineal and rectal region. Six days after admission edema of the left leg was noted and this became more marked each day. A very definite change for the worse was evident on December 18. There was marked dyspnea, anorexia, and the face and extremities took on a bluish pallor.

An abdominal mass was palpated reaching the level of the umbilicus. The anus was distended and the mass filled the pelvis and lower abdomen. Signs of definite pneumonic process were present, confirmed by x-ray, due to real pneumonia or metastatic involvement. The child's pulse became imperceptible, her temperature rose to 104° F. plus and she died Dec. 20, 1938, aged 1 year 10 months.

Autopsy.—Gross: Body was that of a female infant, weighing 20 kilograms and measuring 84 cm. in length. It was markedly emaciated. The chief findings were in the pelvic cavity which was filled by nodular hard masses partly extending above the pelvic brim posteriorly. Abdominal wall showed no remnant of the transplanted ovary. In the chest retromediastinal masses were found about 6 cm. in diameter, compressing the esophagus and trachea, and pushing the aorta to the left. Numerous hard lymph nodes 1 to 2 cm. in diameter surrounded the primary bronchi. Both lungs, particularly the right lower lobe, were filled with tumor masses, showing large areas of necrosis. Pelvic organs had to be removed in toto. Only a small portion of the fundus showed normal outlines. The rest of the uterus and the upper portion of the vagina were replaced by fibrous gray growth, invading both the parametria, anteriorly penetrating the bladder and forming a small warty growth over the lower surface of the bladder mucosa. Posteriorly the growth had invaded the rectum, and compressed both ureters and both kidneys. Both kidneys were cystic and on cross section, distended caseous areas were seen containing turbid fluid. The liver weighed 337 Gm., had greenish parenchyma and was studded with smaller and larger nodules varying from 2 mm. to 3 cm.

Anatomic Diagnosis: Carcinoma of cervix uteri with extension to parametria, bladder, and rectum. Metastases to retroperitoneal and mediastinal lymph nodes, lungs, and liver.

Microscopic section of the primary mass and metastases showed identical appearance, with a glandular growth of low cuboidal cells showing marked anaplasia and very numerous mitotic figures.

Microscopic Diagnosis: Adenocarcinoma of cervix uteri with metastases.

I wish to express my thanks to Dr. J. Heilbrun, to whom the bleeding was first reported and who referred the patient to me; to Dr. J. Faison and his associates, who provided and applied the special radium applicators, and to Dr. N. M. Alter, who followed most avidly the pathologic changes and developments.

39 GIFFORD AVENUE

Bukowski, R.: Clinical Studies in Hystero-Salpingography, Arch. Gynäk. 168: 775, 1939.

The author analyzes the results obtained in a series of 253 hysterosalpingographies. There was 1.6 per cent higher incidence of closed tubes when the test was carried out during the premenstrual period. Pre-existing pelvic infection was reactivated in 7 women in spite of careful observation of the contraindications to the test. A group of six women in whom tubal implantation had been performed, were followed roentgenologically over long periods. In 5 the tubes remained patent and two of these had successful pregnancies following reimplantation. Bilateral tubal occlusion was found in 30 per cent of the 60 women with primary sterility and in 48 women with relative sterility. Tubal pathology was found in 49 per cent of 94 women with other gynecologic complaints; almost half of these showed bilateral tubal occlusion.

In grouping the entire series, 27 per cent showed bilateral tubal occlusion. These could be explained on the following basis: 14.6 per cent followed a febrile puerperium, 26 per cent followed abortion, 18 per cent were nonspecific in origin, 13 per cent followed gonorrheal infections, and 9.8 per cent were secondary to appendicitis.

RALPH A. REIS.

ACUTE ANTERIOR POLIOMYELITIS COMPLICATING CARCINOMA OF THE CERVIX IN A THIRTY-YEAR-OLD FEMALE

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Kingston Avenue Hospital)

W. S., a 30-year-old white female, was admitted to the Kingston Avenue Hospital on Oct. 6, 1939, complaining of inability to move both lower extremities. Her family history was irrelevant except that her mother died in her early forties of cancer. Menstruation began at the age of sixteen and was irregular, moderate in amount and of 4 to 5 days' duration. She had one child, seven years old, delivered spontaneously. Two induced abortions preceded her delivery in the space of two years. Her past history dates back to October, 1937, at which time she noticed spotting between her otherwise normal menstrual periods. The bleeding gradually increased in intensity. After three months she consulted a private physician who diagnosed a tubal pregnancy and gave her heat therapy for one month. The metrorrhagia continued and the patient, during the following year, consulted many physicians who recommended various medications. In September, 1938, the patient had a profuse vaginal hemorrhage. This was controlled by packing. The following month she entered a local hospital where a pelvic examination revealed a slightly enlarged uterus, induration of the left parametrium, and a deep excoriating ulcer over the anterior cervical lip. Clinical diagnosis was carcinoma of the cervix, Schmitz III. A biopsy of this ulcer revealed it to be carcinomatous. She entered the Brooklyn Cancer Institute November 3, 1938.

The physical examination was essentially negative except for the pelvic findings. A repeated biopsy of the cervix on Nov. 5, 1938, revealed a transitional cell carcinoma. Urinalysis and blood Wassermann were negative. Blood count revealed a mild secondary anemia. Roentgenography showed no evidence of pulmonary or cardiac pathology or osseous metastasis.

Between Nov. 7, 1938, and Feb. 8, 1939, the patient received a course of deep x-ray therapy of the following factors: 6 pelvic ports (2 anterior, 2 lateral and 2 posterior), 10 by 15 cm., 200 KV, 2 mm. cu. + 1 mm. AL, 50 cm. T.S.D.; 200 r. to 3 areas daily, total 2,400 r. each. Between Feb. 9, 1939, and Feb. 24, 1939, an intravaginal port of contact therapy was given (all factors as above) 400 r. units daily for a total of 4,000 r.

On Jan. 6, 1939, because of continued vaginal bleeding, despite the roentgen therapy, watery discharge and pain in the back which radiated to the left hip and leg, the patient was readmitted to the Brooklyn Cancer Institute. Pelvic examination revealed a slightly enlarged uterus and a moderately hypertrophied cervix. The anterior cervical lip was the seat of a deep ulcer, which was the site of the bleeding. Vaginal as well as rectal examination revealed a dense parametrial infiltration on the left. Biopsy of the cervix on Jan. 20, 1939, still showed a squamous cell carcinoma.

On Jan. 20, 1939, the patient received 3,000 mg. hr. of radium element by means of a tandem, colpostat and cork inserted into the cervix and vagina. Ten days later, an additional 2,000 mg. hr. was administered by the same technique. On Sept. 11, 1939, the patient weighed 116 pounds, a gain of 10 pounds in seven months.

On Sept. 15, 1939, the patient contracted a cold, had malaise the following day, and improved somewhat during the next two days. The following day the temperature rose again, the patient vomited several times, the headache became

severe, and the patient complained of pain in the left knee. Within the next twenty-four hours she developed a stiff neck and a rigid back; the next day a progressive weakness of the left leg appeared. The patient's condition at that time was diagnosed as "grippe." On Sept. 22, 1939, there was clinical evidence of paresis of the right leg. On Sept. 24, 1939, the patient was admitted to Kings County Hospital. The temperature on admission was 100° F., pulse 118, respirations 22, and blood pressure 110/60. The following day a neurologic consultation reported: "There is a symmetrical flaccid paraplegia, left worse than right. There is weakness of the hip, knee, and ankle. Deep reflexes are not elicited. There is no response to plantar stimulation. Abdominals are intact. Sensation is entirely intact, including the saddle. Impression: findings are those of a purely motor disturbance of the lower motor neuron type. The symmetrical character as well as the absence of sensory changes would suggest intraspinal disease, the actual nature or location of which is not clear. It would be difficult to understand how a localized metastatic disease of the spine could give such extensive involvement and yet not produce sensory changes or pain. Involvement of the cauda equina must be ruled out."

On Sept. 26, 1939, it was noted that the patient had not voided for the past twenty-four hours, which suggested the presence of a neurogenic bladder. On Sept. 28, 1939, the patient was transferred to the Brooklyn Cancer Institute where the same findings were noted. A lumbar puncture was performed which revealed the following: Clear fluid under normal pressure with no evidence of intrathecal block. Qualitative globulin was 2-plus, chlorides 705 mg. The Kahn and Wassermann tests were negative. The blood chemistry findings were normal, while the count showed a mild anemia. Urinalysis revealed a faint trace of albumin, 3 to 4 white blood cells per high power field. Roentgenograms of the skull and spine revealed no metastatic or other osseous lesions.

At this stage, the diagnosis of poliomyelitis was entertained and on Oct. 6, 1939, the patient was transferred to the Kingston Avenue Hospital, where physical examination revealed a fairly well-nourished adult female, complaining of pain in the left hip and thigh. The right lower extremity showed partial loss of power of the hip flexors, the quadriceps, and the calf muscles. The left lower extremity was completely flaccid with moderate atrophy. The spinal musculature was weak. There were no sensory changes. Deep reflexes of both lower extremities were absent. A spinal tap was productive of crystal clear fluid under normal pressure, with no evidence of block. There were 25 cells (all lymphocytes) per c.mm. Total protein was 78 mg. per cent; chlorides, 665 mg. per cent; sugar, 59 mg. per cent. There was a faint trace of globulin. No organisms were cultured. Pelvic examination: the vagina showed conical atresia with the fornices obliterated, the cervix was small, smooth, firm and partially fixed. The uterus and adnexa were atrophic (postradiation). Rectal examination showed moderate bilateral parametrial infiltration. The course in the hospital was uneventful and afebrile. Posterior plaster-of-Paris splints were applied to both lower extremities, and, on the eighth day of hospitalization, the patient was transferred to the orthopedic division of Kings County Hospital for physiotherapy.

Further examination revealed that the entire left lower limb was flaccid. There was almost complete paralysis except for the tensor fascia lata which still retained approximately half of its normal function. The right lower extremities showed major involvement of hip flexors, hip adductors, quadriceps, hamstrings and posterior tibial; all other muscles were involved to a minor degree. Removable splints were applied and hydrotherapy was instituted for a period of three months. Baking and massage with gentle passive exercise were later employed. Patient was confined to bed throughout with fixation supportive splints in situ. After this time, the left limb was still flail and the right limb had recovered muscle function from -3* to -1 in all groups. Reflexes remained absent. Atrophy of the left lower limb was one inch greater than the right.

*-4 equals loss of all power.

-3 equals loss of $\frac{3}{4}$ power.

-2 equals loss of $\frac{1}{2}$ power.

-1 equals loss of $\frac{1}{4}$ power.

SUMMARY

A case of acute anterior poliomyelitis complicating carcinoma of the cervix in a 30-year-old female patient is presented. The important features of the differential diagnosis of these two entities are stressed.

COMMENT

This case is of special interest because of the unusual finding of poliomyelitis in association with carcinoma of the cervix. Poliomyelitis in adults is very rare. The incidence was 0.6 per cent of the reported cases during the 1931 epidemic in New York City. The diagnosis of poliomyelitis was delayed in this case because a carcinomatous metastasis to the spine appeared to be a more likely possibility, especially in view of the pathologic diagnosis of carcinoma of the cervix following biopsy and the presence of paralysis, atrophy, and neurogenic bladder. However, the complications of a carcinoma of the cervix are usually those of induration and infiltration of the parametrium implicating the ureters and leading inevitably to a progressive and fatal hydronephrosis. Second, metastasis of carcinoma of the cervix to the skeletal system is quite rare. As far as can be ascertained in the literature, neurogenic bladder due to a metastasis of carcinoma of the cervix seldom occurs. The fact that the paralysis developed in an acutely ill patient who presented signs of meningeal irritation accompanied by characteristic changes in the cerebrospinal fluid, in addition to the involvement of scattered muscle groups and absence of sensory changes, was significant enough to have invited the suspicion that these were manifestations of a condition arising *de novo*. Moreover, the onset of this clinical picture coincided closely with the height of the seasonal incidence of poliomyelitis.

600 ALBANY AVENUE

UNFAVORABLE SULFANILAMIDE REACTION AND BLEEDING DUODENAL ULCER COMPLICATING A PUERPERIUM

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Service and Ideal Hospital)*

THIS case is reported because of the unusual picture of a severe gastrointestinal hemorrhage in the puerperium already complicated by pyelitis and an unfavorable sulfanilamide reaction.

V. M. (No. 31465), aged 39 years, gravida viii, para vii, was admitted to Ideal Hospital at 6:50 P.M. Dec. 2, 1939. A previous history is inadequate because of a very marked speech defect, but a subsequent study of the record showed nothing abnormal during the ante-partum course. The patient's blood pressure, blood count, and urine were normal eleven days prior to admission. Medical histories were located and studied back as far as 1934. They showed only a number of minor medical complaints and a history of one severe pyelitis in 1934 which required hospitalization. In these records there was no mention of gastrointestinal complaints or disturbances of any type. On admission, the patient had slight irregular contractions for twelve hours and developed a very marked abdominal distention. A physical examination showed a vertex presenting, fetal heart good, blood pressure normal. The pains became more frequent but were of poor quality. The patient was unable to void at any time. At 9:25 A.M. a catheterized specimen showed four-plus albumin and free blood and a culture was reported as loaded with *B. coli*. Labor progressed very slowly. The pains were irregular and of very poor quality although the patient complained bitterly both during and between contraction. Labor was terminated by low forceps shortly after full dilatation. Only moderate

traction was used. About 50 c.c. amniotic fluid stained with dark red blood followed delivery. There was a fetal heartbeat but no respiratory response to use of stimulants or resuscitator. The placenta did not show any definite location of premature separation. Autopsy of the infant showed a large subcapsular hemorrhage on the inferior surface of the liver and a diffuse hemorrhage into the right adrenal gland. The puerperium was stormy throughout.

The first three days there was marked abdominal distention with some right flank tenderness. Temperature 100° to 101° F., pulse 130 to 140. On the fourth day the patient passed a copious tarry stool. The red count was 3,620,000, Hg, 65 per cent; white count, 11,050; and polymorphonuclears, 90 per cent. Sulfanilamide was started. The next two days there were frequent large intestinal hemorrhages. Transfusions were given daily, yet the red count was down to 1,970,000. Eighty grains of sulfanilamide had been given over a period of forty hours and a check on the white count showed a drop from 11,050 to 4,100. The polymorphonuclears went down to 40 per cent. The patient's general condition was decidedly worse. Because of the subcapsular and adrenal hemorrhages in the infant, the possibility of a blood dyscrasia was considered. Bleeding and clotting time, clot retraction time, fragility test, and prothrombin content were all within normal limits. Transfusions were continued but on the eighth day post partum bronchopneumonia developed and the patient died. Shortly before death, the red count was 1,860,000; Hg, 47 per cent; white count, 1,850; polymorphonuclears, 60 per cent.

The essential parts of the autopsy report are:

Peritoneal Cavity: The most important feature presenting itself was a marked gangrene of the retroperitoneal tissues.

Heart: This organ appeared of normal size but was very soft and flabby. The subcardial fat was moderate in amount. The coronary arteries appeared patent and free from visible degeneration. The mitral valves showed definite, healed fibrous thickenings along the line of closure. The other valves were not remarkable. The myocardium was uniform in color and consistency, being of a dull brownish color and soft.

Lungs: The lungs showed indication of consolidation throughout all lobes. The picture, most pronounced in the lower lobes, was that of a bilateral pneumonitis.

Spleen: Grossly, the picture was that of a marked toxic splenitis and passive congestion.

Gastrointestinal Tract: Duodenal ulcer. No obstruction was found throughout the length of this tract. The extreme gaseous distention without obstruction from feces or abnormality of wall indicated paralytic ileus. The stomach was negative. A definite pear-shaped, shallow ulceration was noted in the duodenum about 1 cm. distal to the pyloric sphincter. The ulceration was about 8 mm. long and half as wide. The duodenal mucosa was congested for a considerable distance beyond the ulceration. An examination of the mucosa throughout the rest of the tract showed no features of interest grossly.

Liver: A marked degree of parenchymatous degeneration was indicated together with toxic hepatitis.

Kidneys: Weights: each weighed 227 Gm. The capsule of each stripped clean but not easily. The surfaces revealed were pale and smooth and mottled by fine grayish, closely set foci. The cut surfaces of each were similar and showed a corticomedullary portion narrower than normal, due to distinct and fairly marked pelvic dilatations characteristic of moderate hydronephrosis. The kidney cut surfaces were paler than normal with some slight indistinctness of the architectural markings suggestive of inflammatory change.

Ureters: The lower portions of each ureter were lost in the mass of necrotic tissue in the pelvis and were not traced.

Bladder: On section it gave the impression of acute cystitis.

Genitalia: The uterine cervix was deeply congested, red in color and swollen, features which also characterized the entire vaginal mucosa with which it blended. A rent in the friable vaginal wall on the right side was noted after removal. Because of the friability of the vaginal tissue and because this opening was not noted during preliminary examination of the vagina and uterus in situ, the assumption

was that it resulted from immediate manual manipulation. It was, however, possible that the infection which appeared to be a descending one, had previously perforated the vaginal wall, either with or without a distinct opening. Roughened areas of endometrium were present in the upper portion of the uterine cavity. This tissue appeared necrotic and discolored and was connected with the vagina by injected streaks along the endometrium. The remainder of the endometrium was not remarkable and grossly showed no evidence of being involved in the infectious process. The uterine wall, while boggy, showed no visible evidence of being infected on sectioning.

Microscopic examination showed:

Lungs: The sections showed the presence of an acute bronchopneumonia associated with marked edema of the lung tissue and engorgement of blood vessels, large and small. Microscopically, the picture was that of a terminal hypostatic bilateral pneumonitis.

Gastrointestinal Tract: Duodenum sections showed an ulceration in the mucosa which had excavated down to the submucosa. The base of the ulcer was necrotic and hemorrhagic. An active inflammatory reaction associated with the ulcer was exhibited by a diffuse infiltration of the duodenal wall by eosinophiles and lymphocytes. The wall was also markedly edematous. The serosal aspect of the duodenum was actively inflamed. Sections from other portions of the intestinal tract showed necrosis of the superficial aspects of the mucosa and a marked diffuse inflammatory reaction throughout the submucosa, muscularis, and adventitia.

Kidneys: The right kidney showed a moderate pyelonephritis. This was shown by foci of both acute and chronic inflammatory cells in the kidney which were present in various parts of cortex, medulla, and renal pelvis. In these areas, destruction and fibrous replacement of glomeruli had taken place; tubules were damaged and contained necrotic debris and bacteria. The damage was moderate in degree, as much of the kidney revealed only parenchymatous degeneration and edema. In the ordinary case of this sort it was possible to consider the infectious process as an ascending one. In this case, the picture was complicated by the fact that the perirenal tissues, which were markedly actively inflamed, communicated through a break in the kidney capsule with the most actively inflamed areas within the kidney. One could surmise without settling the question definitely that infection entered the kidney from without, or on the other hand, that infection originated within the kidney and involved the capsule secondarily, or still further, that the two processes started independently and joined forces. The most alluring one to me as I review the evidence is that an infection originated in the duodenal ulcer and spread from there to the kidney and also down the psoas to the pelvis.

Uterus: The roughened area of the uterine cavity microscopically was seen to be the seat of distended venous sinuses filled with clot, associated with atrophic and necrotic endometrium. There was evidence of moderate acute inflammation in the area. The uterine musculature underlying this area was loose and edematous but apparently free from infection. The cervical tissues and the vaginal wall were necrotic and very acutely inflamed. It seemed inevitable that the poorly nourished endometrium should become infected, but the condition of the uterine wall and the remainder of the endometrium indicated that the process was incidental and secondary and not a primary source of the pelvic and other pathology.

CONCLUSION

After studying the history and seeing the autopsy, I feel that here the pregnancy was incidental to two underlying conditions: namely, pyelitis and duodenal ulcer. The duodenal ulcer hemorrhage plus the unfavorable reaction to sulfanilamide were a most unfortunate combination and were definitely contributory to her death. Sulfanilamide, although a great advance in therapy, is a drug to be used only with caution and the blood count must be followed very closely throughout its administration.

This case illustrates the well-known, but often forgotten fact that pregnant women do suffer from any and all medical complications.

FRIEDMAN TESTS WITH OVARIAN PREGNANCY*

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WILMINGTON, DEL.

OVARIAN pregnancies are sufficiently rare to warrant reporting each case history. The case to be reported is of special interest, owing to a record of two positive Friedman tests during the first two months of pregnancy followed by a negative test shortly before surgery was advised.

Mrs. E. G., aged 25 years, consulted one of us (V. S.) on June 3, 1938, at which time she gave a history of a sudden severe pain in the lower abdomen on the night of June 1, at a time when her menstrual period was overdue two weeks. Her menstrual periods began at the age of 14 years and had been regular twenty-eight-day type, lasting four days, usually without pain. She had been married five years and the only period she could recall missing in the past had been in September, 1937. Her past medical history was negative except for measles, mumps, and scarlet fever as a child, and she had passed a urinary calculus in 1935 after several attacks of renal colic. The attack of pain on the night of June 1 was severe, and at its onset she felt faint and was unable to lie flat without an exaggeration of the distress. However, it gradually disappeared, a physician's services not being secured, and she came for an examination to determine if she was pregnant. The general examination was essentially negative except for an unusual growth of hair on her body and a male type of distribution on her abdomen. The external genitals were negative. On bimanual examination the uterus was found to be retroverted, slightly enlarged, and softer than normal. The left adnexa seemed normal, while the right appeared to be adherent to the side of the uterus. Pregnancy was suspected but a definite diagnosis could not be made. The patient was very anxious to know whether or not she was pregnant and a week later when it was still impossible to make a definite diagnosis a Friedman test was advised. This test was reported positive on June 13. On July 20, she reported that there had been some irregular bleeding during the past two weeks. Daily injections of progesterin were given for ten days. On July 26 another Friedman test was reported positive. However, she had only short intervals of freedom from an offensive, red vaginal discharge which lasted about five weeks. Bimanual examinations on August 22 and September 12 showed that the uterus was not enlarging normally. On September 24 she reported that after freedom from discharge for four weeks there had been five days of what seemed to be a normal menstrual flow. Bimanual examination at this time showed no evidence of uterine enlargement, but there was a tender mass at the right side of the uterus. A Friedman test was reported negative on September 27. It was believed that she had a right-sided ectopic pregnancy, but the possibility of an ovarian neoplasm was considered. Surgery was advised. On opening the abdomen on October 6, both tubes appeared normal, but both ovaries were enlarged and adherent. The larger right ovary was 5.5 cm. in diameter and its appearance suggested endometriosis. The left ovary while smaller was cystic and adherent to the pelvic wall. The right ovary was removed and the left ovary resected. A grossly normal appendix was removed by request. At the time of the operation, it was believed that she must have had a uterine abortion during July or the first days of August, and that she had an endometriosis of the right ovary.

The report of the pathologist was as follows: "Gross: Ovary enlarged to a diameter of 5.5 cm. by a dull red mass resembling old blood clot. A second

*Presented at a meeting of the Obstetrical Society of Philadelphia, January 4, 1940.

smaller piece of cystic ovary is also submitted. Normal appearing appendix 6 cm. long. Microscopic: The hemorrhagic mass from the ovary consists of old blood clot adjacent to ovarian tissue. The section indicates that the blood clot is adherent to the ovary rather than having originated within the organ. Numerous amorphous, blue staining masses have the appearance of necrotic chorionic villi, but no decidual cells are recognizable. *Diagnosis:* Suggests ectopic pregnancy." Following this report further sections were studied and in one a villus was found that seemed to be attached to ovarian stroma (see Fig. 1).

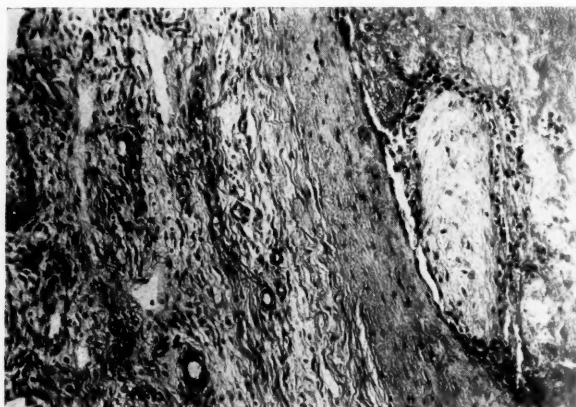


Fig. 1.—Photomicrograph showing villus apparently attached to ovarian stroma. Shadows of degenerating villi were found in the blood clot that made up a considerable part of the ovarian mass.

Our final diagnosis in this case was ovarian pregnancy with death of the embryo and beginning absorption of the products of conception. Whether this was a primary or a secondary ovarian pregnancy cannot be determined. It is possible that this patient had a tubal abortion at the time of her abdominal distress on the night of June 1, the early fertilized ovum becoming attached to the ovary at the site of rupture of the follicle from which the egg escaped. The two positive Friedman tests, on June 13 and July 24, indicate that embryonic development must have continued for at least two months. Death of the embryo may have resulted from an inadequate blood supply. Our findings at the time of operation suggest a gradual absorption of the products of conception and if the operation had been delayed several weeks longer, it is possible that no evidence of the pregnancy would have been found. The findings in this case suggest that an ovarian pregnancy may be missed very easily.

Fortunately this patient became pregnant again early in July, 1939, and she apparently has a normal intrauterine pregnancy.

Nogues, A. E., and Gazzotti, C. L.: Mammography, Rev. méd. latino-am. 24: 999, 1939.

The technique and difficulties of mammography are described by Nogues and Gazzotti. They used colloidal thorium dioxide. No unfavorable reactions were traceable to the injections. Mammography has an important place in the diagnosis of intracanalicular tumors as well as being of localizing value for any processes involving the ducts. It is an important adjunct test in paraductal tumors. It should be used routinely in all cases of abnormal nipple secretions not amenable to usual treatment. An excellent series of radiographs is presented.

R. J. WEISSMAN.

HEMORRHAGE IN THE LATE PUERPERIUM*

HERMAN A. STRAUSS, M.D., CHICAGO, ILL.

HEMORRHAGE in the late puerperium is usually pelvic in origin and rarely due to a blood dyscrasia. The presence of such a true blood dyscrasia usually manifests itself during labor and/or the immediate puerperium. Delayed manifestations resulting from such a dyscrasia are sufficiently uncommon to warrant the following report.

The patient, A. W., a white, 26-year-old primigravida, at term, was admitted to the Michael Reese Hospital in the first stage of labor on Oct. 19, 1938. Her pregnancy had been uneventful, the Wassermann test negative, and there was nothing in her history or physical findings suggestive of blood dyscrasia.

After thirty-six hours of labor, the heart tones, which had been 160, became somewhat irregular and dropped to 116-128. Cervical dilatation at this time was 7 cm. with the head at the level of the ischial spines. An hour later the heart tones became very irregular and slow, and it was therefore decided to terminate labor. Dührssen's incisions of the cervix were made at "two" and "ten o'clock," a deep mediolateral episiotomy was done, and the fetus extracted by midforceps. A right sulcus tear resulted which was repaired together with the Dührssen's incisions and the episiotomy. The patient made an uneventful recovery. She was out of bed on the eighth day and left the hospital on the eleventh day.

Three days after discharge from the hospital the patient began to bleed vaginally. Speculum examination revealed the cervix well healed with no evidence of bleeding from the canal. The impression at this time was that of delayed post-partum hemorrhage. Two days later the bleeding became profuse. A curettage was done, and a small amount of decidual tissue was removed. No placental tissue was found. Five days after the curettage, profuse bleeding recurred. Speculum examination now revealed bleeding from a pin-point area in the suture line of the right sulcus tear. This was located in the middle third of the vagina. The suture line had healed by primary union, and there was no sign of infection. No evidence of the suture line other than that similar to a scratch made by a pinhead on the skin could be seen.

Between November 16 and December 14 (fifth to ninth week post partum), this vaginal mucosa was sutured five different times for recurrent bleeding, using both catgut and silk. The ligatures controlled the bleeding from two to five days. Vaginal packing was used in the intervals between the various ligations, and when the patient lost blood faster than transfusions could replace it, resuturing was done. On occasion two transfusions of 500 c.c. of whole blood were given in a single day. On November 30, twenty-three days from the initial bleeding, the clotting time was prolonged for the first time from one and one-half to nine minutes. On December 3, the right internal iliac artery was ligated through an extraperitoneal approach.¹ Bleeding was decreased for only eight hours. On December 4, bleeding was again out of control and the left internal iliac artery was ligated. On December 6 the red blood count had dropped to 1,360,000, the platelets were 150,000, clotting time was ten minutes, and bleeding time was twelve minutes. Although the bleeding was not stopped, it had decreased markedly and was under control after ligation of both internal iliac arteries. Five days after the right ligation a large hematoma appeared in the right inguinal wound. On December 14, consultation with Dr. S. O. Schwartz, hematologist at Michael Reese Hospital, brought forth the suggestion that constitutional capillary fragility was a factor in the bleeding. Moccasin snake venom was therefore used, being administered subcutaneously. On December 15, blood standing for twenty-four hours did not coagulate. A large hematoma now appeared in the left inguinal incision (fourteen days post-operative). The irritation from constant changing of cotton packing one to two

*Presented at a meeting of the Chicago Gynecological Society, January 19, 1940.

times a day to control bleeding started active bleeding from the intact anterior vaginal vault. Packing was stopped on December 18, and kephrine hydrochloride (methylaminoacetatechol hydrochloride) was blown into the vagina by means of a Wyeth blower. The powder was applied from one to six times daily (as often as bleeding appeared). Within six days after the use of this powder, the bleeding practically ceased. By January 4, two months from the onset of hemorrhage, the bleeding stopped completely. At this time the hemoglobin was 60 per cent (Sahli), and the red blood count was 3,600,000.

During these two months the patient had been given sixteen blood transfusions varying from 500 to 700 c.c. of whole blood. On February 5, three months from the onset, the patient was discharged from the hospital after being up and about for two weeks. Three days after leaving the hospital she developed a large ecchymotic area extending from the right hand to the elbow. There was no history of injury. On February 15, the patient was admitted to Mount Sinai Hospital for blood studies. The outstanding findings were clotting time, 75 to 100 minutes, and prothrombin time eight times greater than normal. Subsequently the patient developed ecchymotic areas on the legs as well as the abdomen. The last week in February the patient had what she described as a normal menstrual period lasting four days. On March 4, two months after all bleeding had ceased, the vaginal mucosa was inspected, was found to be well healed, and the silk sutures were removed. The patient was up and about and doing her usual household duties but continued to develop spontaneous ecchymotic areas on different parts of her body.

On April 20th a blood study was made by Dr. Gurth Carpenter, of the University of Chicago. The platelet count was 290,000, clotting time one and three quarter minutes, bleeding time two minutes, red blood count 4,880,000, normal white and differential counts. In his report Dr. Carpenter stated: "I emphasize the fact that our investigations were not complete on the basis of one visit. It is my impression that this case belongs to that ill-defined, poorly described bleeding tendencies associated with endocrine dyscrasias." This blood picture was obtained nine days prior to the death of the patient.

On April 29 she entered Mount Sinai Hospital with the history of having been bitten on the tongue. The tongue was found to be tremendously swollen and occupied the entire oral cavity. A tongue depressor could not be inserted between the tongue and the roof of the mouth. The tongue was blue red in color, and there were clots of blood in the oral cavity. The submental, submaxillary and thyroid areas showed hemorrhagic distention of the underlying structures. The patient had marked dyspnea, requiring use of the accessory muscles of respiration. A tracheotomy was done by Dr. M. R. Guttman to relieve the respiratory embarrassment. The patient's condition remained good for about six hours after the tracheotomy. This was followed by sudden massive hemorrhage and the patient literally drowned in her own blood. No autopsy was obtained.

CONCLUSIONS

In view of the patient's history, the type of response to treatment, and the final outcome, it is believed that this patient must be placed into that group which has been classified as "constitutional capillary fragility."

REFERENCE

- (1) *Leventhal, M. L., Lash, A. F., and Grossman, A.*: Surg. Gynec. Obst. **67**: 102, 1938.

INVERSION OF THE PREGNANT SIDE OF A DOUBLE UTERUS

LEROY E. BATES, M.D., SAN ANTONIO, TEX.

(From the Gynecological and Obstetrical Service of the Santa Rosa Hospital)

THE following case constitutes an unusual complication of pregnancy in a double uterus.

Mrs. C., aged 18 years, first came to me when she was six months pregnant. Her past history was uninteresting, except that she had had a previous spontaneous abortion at six weeks. All of her pelvic measurements were within normal range and a vaginal septum was discovered at the time of her first examination. It was thought that a bicornuate uterus was present. The pregnancy occurred in the left side as is usually the case when this anomaly is present.

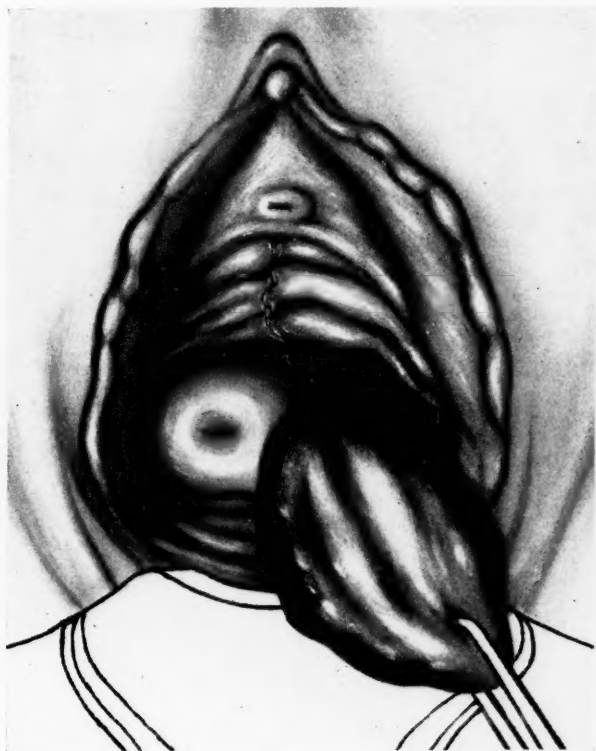


Fig. 1.

She went into labor at seven months and delivered an apparently normally formed premature infant. Her delivery was remarkably easy, but the vaginal septum ruptured at the time. No difficulty was experienced with the delivery of the placenta. Traction was not exerted on the cord.

She did not lose an unusual quantity of blood at the time of her delivery and suffered absolutely no shock. For the first week her puerperium was entirely normal and she got out of bed on the eighth day. A day or two after she was up and around the house she began to bleed. She was put back to bed and given ergot for several days without any improvement.

Twenty-four days after delivery she was taken to the hospital with the intention of doing a curettage to control the bleeding. On inserting a speculum into

the vagina, a polypoid tumor was found attached to the cervix. This tumor was about three inches long and about an inch in diameter at the largest point. No tubal opening was apparent, and it was felt that we were dealing with a fibroid. An attempt was made to snare this tumor off, but the snare would not cut through it. The cavity of the uterus was definitely made out on the right side.

Very little bleeding occurred after removal of the tumor, but a light pack was inserted up to the operative wound.

The pathologist reported that the ovary, tube, and uterus had been removed.

I have no idea when the inversion of the uterus occurred. It would have been impossible to have replaced this uterus without incising it longitudinally, as complete involution had taken place with the uterus in the inverted position.

A most interesting fact was the absence of bleeding from the cut uterine and ovarian arteries, and the total absence of shock from the inversion of the uterus.

1234 NIX PROFESSIONAL BUILDING

ECLAMPSIA ASSOCIATED WITH PLACENTA PREVIA*

FREDERICK A. WURZBACH, JR., B.S., M.D., NEW YORK, N. Y.

THE association of eclampsia and placenta previa is apparently a very rare obstetric condition. A review of the literature for the past forty years reveals only three reports. The first in 1904 is in an Italian journal not available in this country. The second is a report in 1910 by M. Plauchu of Lyon, France, where, because of oligohydramnios, he punctured through the placenta, draining the fluid, and, after dilatation was effected, did a craniotomy and extracted the child. This mother lived. The third case is one reported in 1921 by Douglas Miller, from the Royal Maternity Hospital, Edinburgh, of a postpartum eclampsia three days after a version and breech extraction for complete placenta previa. The mother and child both died.

CASE REPORT

E. W., 25 years old, white, gravida ii, para 0, had a miscarriage at four months on Aug. 11, 1936. The last regular menstrual period occurred on Oct. 25, 1936; due date Aug. 2, 1937.

She was a regular attendant at the Pre-natal Clinic of Morrisania City Hospital from March 24, 1937, to June 9, 1937. At this last visit her blood pressure was 120/80. Her urine was negative and she had no complaints. The Wassermann and Kahn tests were negative. At 7:00 P.M. on the evening of June 21, 1937, her husband returned from work and found the patient lying on a couch in a pool of blood and in a comatose state. She was admitted from a public ambulance to our emergency room at 7:30 P.M.

On admission she was restless, irritable, and semistuporous. Almost immediately she had a generalized convulsion lasting several minutes. She was admitted to the open surgical ward under the care of the obstetric division. This was necessary as our wards were closed, and she was too critical to be again transported to any other hospital.

The past history was negative. The recent history revealed that for five days she had complained of headache, nausea, vomiting several times a day, puffiness of the face, and swelling of the ankles. She had not returned to the clinic and had relied on the self-administration of "headache powders."

Physical examination revealed a comatose patient in acute distress. Her face and eyelids were markedly edematous with a parchment feel to the skin. The pupils were widely dilated and reacted moderately to light. The eye grounds

*Presented at a meeting of the Section of Obstetrics and Gynecology, New York Academy of Medicine, Feb. 27, 1940.

showed a few old and new retinal hemorrhages, constricted arteries with indentations of the veins but no blurring of the disks. The ears, nose, and throat were normal. Her tongue was thick, swollen, beefy red and showed several fresh, bleeding wounds. The neck was not rigid. There was no cardiac pathology. The blood pressure (after the convulsive seizure) was 148/108, the pulse was 88 and the temperature 100.8° F. The lungs were clear throughout. The abdomen revealed an eight months' uterus, not ligneous and contracting occasionally. Fetal heart sounds could not be heard. There was much dried blood on the vulva and inner surfaces of her thighs. There was moderate edema of the forearms, hands, legs, and feet.

Immediate treatment was instituted for the eclampsia, consisting of 0.5 gr. of morphine sulphate stat and 0.25 gr. to be repeated every two hours as indicated, 50 c.c. of 50 per cent glucose and 30 c.c. of 10 per cent magnesium sulphate by vein. For the bleeding the foot of the bed was elevated, and there was immediate blood workup, typing and cross-matching of donors.

This treatment controlled the convulsions. Two hours after admission a vaginal examination was done with a donor ready. The vagina was found full of clots. The cervix was thick, soft, and one finger dilated. Placenta was felt covering the internal os. The head could be felt through the cervix anteriorly, and the placenta was believed to be for the most part on the posterior wall of the uterus. The membranes were intact. There was a continuous trickle of blood but no further massive hemorrhage.

The laboratory findings were red blood cells 5,500,000, hemoglobin 80 per cent. The husband was a compatible donor. The urine showed four-plus albumin, many fine and coarse granular casts, and many white blood cells. Urea nitrogen was 0.34 mg. per cent; sugar 75 mg. per cent.

The patient was in a desperate state and continued to bleed. It was believed that since the eclampsia was being controlled the best chance the patient would have for recovery would be a cesarean section, even though the fetus was dead. Three hours after admission a rapid classical section was performed and the dead fetus extracted. The placenta was found covering the internal os and posterior lower surface of the uterus. The uterus was packed and contracted well. Before and during the operation the patient received 700 c.c. of blood by citrate method.

Following the operation the patient had a stormy three days and required considerable stimulation by coramine and caffeine sodium benzoate. One-sixth grain of morphine sulphate and an ampoule of prostigmine every four hours were continued until the third day. One day after operation temperature was 101° F., the pulse 120, and blood pressure 138/74. The second day the temperature was 104° F., pulse 130, and blood pressure 190/138. Thereafter the temperature and pulse gradually fell and were normal by the seventh postoperative day. The edema was gone by the fourth day. The blood pressure receded slowly and was 120/90 on the tenth postoperative day. On discharge from the hospital on the twenty-eighth day, the wound was healed, her blood pressure was 126/88, and the urine still showed a trace of albumin, occasional red blood cells and white blood cells, and granular casts. The patient did not return for post-partum examination.

REFERENCES

- (1) *Nottari, E.*: *Arte-ostet.* Milano 18: 358, 1904. (2) *Plauchu, M.*: *Bull. Soc. d'obst. de Paris* 13: 195, 1910. (3) *Miller, D.*: *J. Obst. & Gynaec. Brit. Emp.* 28: 306, 1921.

CANCER OF THE CERVIX IN A VIRGIN WITH INTACT HYMEN*

A. F. LASH, PH.D., M.D., CHICAGO, ILL.

(From the Michael Reese and Cook County Hospitals)

THE occurrence of carcinoma of the cervix with uterine fibromyomas is well known, the incidence being 1 to 2.6 per cent according to various series of fibroid studies published. Mattmuller found 9.7 per cent of nulliparas among 442 patients with cancer of the cervix uteri of whom 10 or 2.2 per cent were virgins. On a study of over 2,000 specimens of uteri, cervixes, and curettings, Davidsohn found carcinoma of the cervix occurring in 0.93 per cent in Jewish women and 6.4 per cent in non-Jewish women.

This patient, A. S., a 40-year-old, unmarried, Jewish woman, entered the Michael Reese Hospital because of pressure and pain in the right lower quadrant, frequency of urination, nocturia, and menorrhagia. Her personal and past history contained nothing of significance, except that her menses began at the age of 13½ years, occurred every twenty-eight days, and remained for seven days, being profuse and associated with clots and some dysmenorrhea.

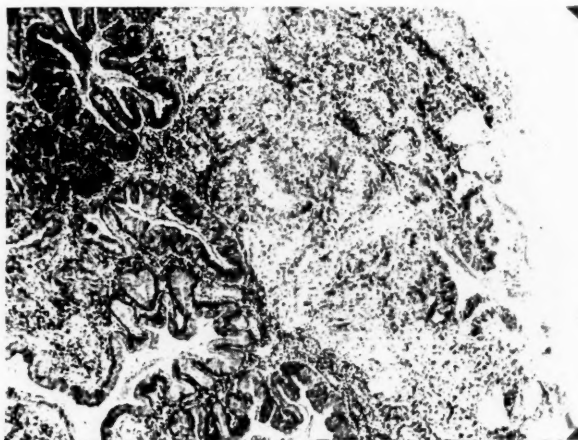


Fig. 1.—Adenocarcinoma of cervix with squamous cell features.

Physical examination showed a normal, small individual, weighing 109 pounds with no general pathology. Pelvic examination was made by recto-abdominal manual palpation because of a tight, intact hymen. The cervix was closed and smooth, the corpus was enlarged to the size of a twelve weeks' pregnancy, hard and free, and the adnexa presented no palpable pathology. A diagnosis was made of fibroids of the uterus.

On Jan. 11, 1939, I performed a subtotal hysterectomy and was surprised to find friable tissue in the endocervix on cutting across the cervix. Therefore, I removed the cervix and both tubes and ovaries. The patient made an uneventful recovery and was given a course of roentgenotherapy. The specimen showed multiple fibromyomas of the uterus with adenocarcinoma of the cervix with squamous cell features.

30 NORTH MICHIGAN AVENUE

*Presented at a meeting of the Chicago Gynecological Society, January 19, 1940.

A SILVER-PLATED VAGINAL PROSTHESIS FOR THE CONSTRUCTION OF AN ARTIFICIAL VAGINA*

BUFORD WORD, M.D., BIRMINGHAM, ALA.

THIS instrument (Fig. 1) was made from the obturator of an old anoscope, being $1\frac{1}{2}$ inches in diameter and $4\frac{1}{2}$ inches in length. The instrument was made by cutting the flange off of the obturator, sealing the open end with a plug and welding on a button, as shown in Fig. 1. The prosthesis was then electroplated with pure silver $\frac{3}{4,000}$ of an inch in thickness over the entire surface. In cases of congenital absence of the vagina, a cavity is created between the bladder and rectum and the

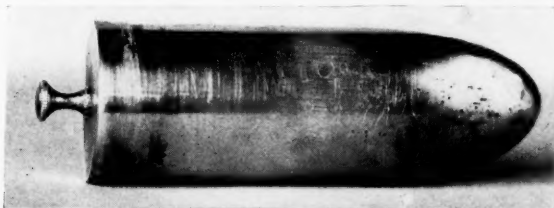


Fig. 1.



Fig. 2.

instrument inserted, to remain until epithelization of the cavity is complete. It may be removed any time after three weeks for inspection. Several pinch grafts of mucous membrane from the vestibule are recommended to be used on the end of the prosthesis to hasten growth of vaginal mucosa. Fig. 2 shows the instrument in place.

I have used the instrument in 4 cases, and it has worked very well. Silver is recognized as a bacteriostatic agent and is also helpful in promoting epithelial growth.

306 MEDICAL ARTS BUILDING

*The above described instrument can be obtained from A. S. Aloe & Company, St. Louis, Mo.

AN AUTOMATIC RECORDING APPARATUS FOR TUBAL INSUFFLATION*

A. HERBERT MARBACH, M.D., PHILADELPHIA, PA.

(From the Obstetric and Gynecologic Service, Jewish Hospital)

MANY instruments have been used to facilitate Fallopian tubal insufflation, and, although all give us the required information, they lack the safety features which are desirable.

The use of compressed gas, coming from a tank into the instrument, has presented many difficulties. Chief among these was the use of a suitable reducing valve to prevent the high pressure in the tank from disrupting the outfit, necessitating many adjustments of the instrument before the test was able to be done. The recording devices in general use employ either a smoked drum or an inked stylus on kymograph paper. Such recordings have been of inestimable value in aiding diagnoses and instituting treatment.

A single dial recording instrument is presented herewith, which satisfies all of the desired and required qualifications for the proper completion of tubal insufflation. This device, in principle, eliminates errors, since personal adjustment is not necessary. The important considerations in devising the instrument were mechanical efficiency and safety, which in previous instruments have been lacking.

Carbon dioxide from the main supply tank is under 750 pounds pressure. By means of a safety control reducing valve, this pressure is cut down to 10 pounds before going to the patient. The rate of flow of the gas through this instrument is automatically regulated at 60 c.c. per minute, and with the instrument in operation, a pressure of 100 mm. of mercury is attained in thirty seconds.

Added to this instrument is a safety valve which does not allow the pressure within the Fallopian tubes to exceed 230 mm. of mercury. This safety device is an essential and component part of the instrument.

The single control feature of the mechanism makes for ease and certainty in doing tubal insufflation. From this one point of control the operator can do the test for diagnostic purposes or give a therapeutic insufflation.

The machine consists of the following parts: (1) A tank of compressed gas (CO_2), (2) a syphon meter bottle, (3) a clock mechanism precision kymograph, (4) a reducing valve, (5) two special valves, and (6) a safety valve.

1. The compressed gas (CO_2) is the medium introduced to determine patency.

2. The syphon meter bottle measures the amount of gas which has passed through the cannula. This bottle is so constructed that with each bubble 30 c.c. of carbon dioxide are delivered in thirty seconds.

3. The kymograph is an aneroid recording manometer. Depending on the resistance to the insufflated gas, the pen on the kymograph rises and records the pressure in millimeters of mercury. The chart on the kymograph is graduated along the radius in millimeters of mercury and around the circumference in minutes of time.

4. The reducing valve brings the pressure within the supply tank from 750 pounds pressure to 10 pounds pressure.

5. Two special valves are used to prevent the pressure from rising beyond the outside limit of 15 pounds, and to control the evenness of the flow to the cannula.

6. A safety valve which automatically stops the flow of gas through the instrument after a pressure of 230 mm. of mercury has been reached.

*Presented at a meeting of the Obstetrical Society of Philadelphia, January 4, 1940.

Two gauges are visible on the panel of the instrument. The one on the left indicates the amount of carbon dioxide present in the supply tank. The other indicates the number of pounds pressure the gas is being delivered to the cannula.

The single control dial has three positions for use. The "OFF" position, in which no gas is flowing through the system and the kymograph is not recording. The "ON" position, in which the gas flows through the system and the kymograph is in operation. The "TREATMENT" position, at which time the kymograph

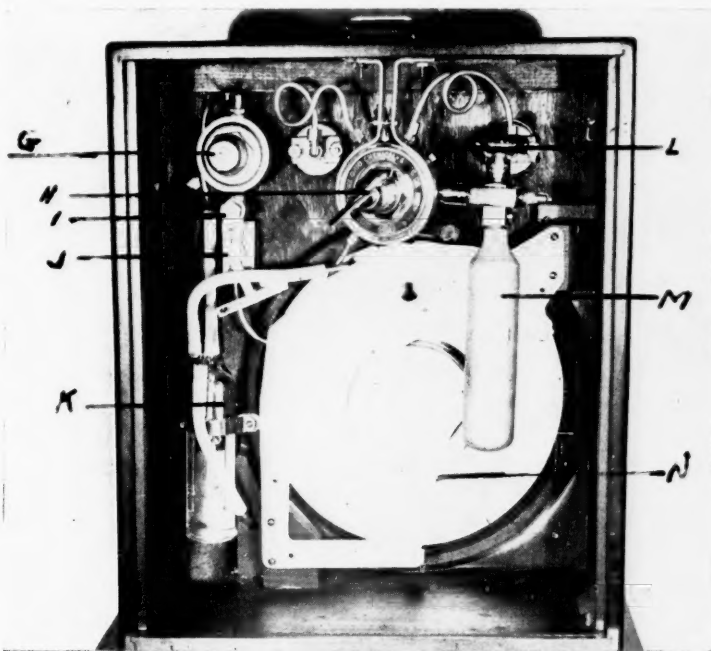


Fig. 1.—Interior view of mechanism. *G*, Safety valve which prevents pressure from exceeding 220 mm. *H*, Regulator to keep pressure in system at 10 pounds level. *I*, Valve to control flow to 60 c.c. per minute and rise of pressure to 100 mm. in thirty seconds. *J*, Rear view of control dial. *K*, Rear view of syphon meter bottle. *L*, Valve to open CO₂ tank. *M*, CO₂ Supply tank. *N*, Rear view of kymograph.

is in operation but no gas is flowing. This "treatment" position is used for therapeutics, since the operator can change the optimum pressure desired with the dial set at "on" and then when the pressure has been reached the dial is set at "treatment." This maintains the pressure within the tubes at a constant level, and we may record the time the treatment has been given.

At the bottom of the panel is a Luer connection into which the cannula tubing is placed.

The procedure then for doing a tubal insufflation with this apparatus is as follows: (1) Open the main supply tank (CO₂), (2) attach the cannula to the Luer connection, (3) turn the control dial to "on" after the cannula has been inserted into the cervical canal.

Instrument made by W. and G. Scientific Instrument Co., Philadelphia, Pa.

255 SOUTH SEVENTEENTH STREET

Society Transactions

NEW YORK OBSTETRICAL SOCIETY

MEETING OF JANUARY 9, 1940

The following papers were presented:

Sex Hormones in Carcinogenesis. Dr. Cornelius P. Rhoads (by invitation).

Carcinoma of the Cervix in a Seven Months Old Infant. Dr. Edward G. Waters. (For original article, see page 1055.)

OBSTETRICAL SOCIETY OF PHILADELPHIA

MEETING OF JANUARY 4, 1940

The following papers and case reports were presented:

Friedman Tests With Ovarian Pregnancy. Drs. Carl H. Davis and V. Stevens-Young. (For original article, see page 1063.)

An Automatic Recording Apparatus for Tubal Insufflation. Dr. A. Herbert Marbach. (For original article, see page 1072.)

An Experiment in Cancer Control. Drs. Catherine Macfarlane, Faith S. Fetterman and Margaret C. Sturgis. (For original article, see page 983.)

Results of Treatment in Carcinoma of the Uterine Cervix. Dr. Roscoe W. Teahan (by invitation) and Dr. Hoke Wammock. (For original article, see page 995.)

CHICAGO GYNECOLOGICAL SOCIETY

MEETING OF DECEMBER 15, 1939

The following papers were presented:

A Clinical Study of Stilbestrol. Dr. M. Edward Davis. (For original article, see page 938.)

Pseudouterus Arcuatus and Functional Malformations of the Uterus. Dr. Louis Rudolph.

Angular Pregnancy. Dr. Ralph E. Campbell and Dr. John L. Parks.

MEETING OF JANUARY 19, 1940

The following papers were presented:

Episodes in the Doctrine of the Three Germ-layers. Dr. George L. Streeter, Baltimore, Md. (by invitation).

Hemorrhage in the Late Puerperium. Dr. Herman A. Strauss. (For original article, see page 1065.)

Cancer of the Cervix in a Virgin With Intact Hymen. Dr. A. F. Lash. (For original article, see page 1070.)

Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D.

Selected Abstracts

Complications of Pregnancy

Solomons, Bethel: *Is It Ever Necessary to Kill a Live Baby?* Brit. M. J. 1: 1175, 1939.

The author discusses the destruction of the fertilized ovum, both intentional and accidental, at all stages of pregnancy.

Hyperemesis gravidarum is considered an indication for terminating the pregnancy only if in spite of thorough treatment for three to five days the Van den Bergh bilirubin reaction is positive, if there is marked albuminuria, if the pulse rate is increasing and the pulse is getting weaker, or if the patient is becoming jaundiced.

A "renal toxemia" occurring from the twenty-fourth to the twenty-eighth week is considered an indication for hospitalization so that the pregnancy may be carried to the point of viability.

Uncompensated cardiac disease is occasionally an indication for induction during the first three months; after this time treatment of the heart condition is indicated. Tuberculosis and renal disease are best treated on medical lines, also Graves' disease except when the patient is rapidly going downhill after about a month of treatment when termination may be considered.

After the twenty-eighth week the author considers the fetus viable and the occurrence of any of the above conditions may be an indication for induction of labor. However, he considers it unjustifiable to perform craniotomy on the live child, particularly since the advent of the comparatively safe lower segment section. The author reports a series of 122 of these cases, 4 of which resulted in maternal deaths.

The author believes physicians kill live babies more often when inertia is present than in any other condition. He classifies inertia as primary and secondary.

The secondary type, due to some discoverable cause, is dealt with accordingly.

The primary type, without discoverable cause, should be treated conservatively and should be interfered with only when labor has lasted from two to four days, when the temperature and pulse rise, and when the fetus shows signs of distress.

The frequency of resort to cesarean section is deplored as is the abuse of the oxytocics.

The author concludes that the fetus should practically never be destroyed.

FRED L. ADAIR AND JOHN NEWDORP.

Cotte and Magnin: *Pregnancy After Myomectomy*, Gynéc. et obst. 39: 210, 1939.

The question of pregnancy after myomectomy is discussed by the writers on the basis of their series of 60 cases of myomectomy. Of the 40 women who were capable of childbearing, 11 had one or more children after the operation. They emphasize that in the women who remained sterile after myomectomy associated lesions present during the operation were responsible for the sterility. Thus, among 33 women in whom the tubes and ovaries were normal at the time of the myomectomy, 10 had one or more pregnancies following the operation. On the other hand, of 8 women who had one tube and ovary removed at the time of the myomectomy because of adnexal disease, only one became pregnant; her case is reported in this paper.

In the authors' total series of 40 cases, pregnancy followed 16 times. Of these, 13 went to term and resulted in living children while 3 terminated in miscarriage. These figures are the best argument in favor of conservative operative treatment of uterine myomas.

J. P. GREENHILL.

Naujoks, H.: Hyperemesis Gravidarum and Ileus in Pregnancy, Ztschr. f. Geburtsh. und Frauenheilk. 1: 60, 1939.

The treatment of hyperemesis gravidarum is still a serious problem; in some cases the condition becomes worse even in spite of emptying of the uterus. In the author's series at Königsberg, among 82 cases of excessive vomiting there were 12 interruptions of pregnancy and 2 deaths, and among 231 cases in Cologne there were only 5 therapeutic abortions and 1 death. In the latter case chronic ileus was present. The author reports additional cases of true ileus and emphasizes the difficulties in making a correct diagnosis. The mortality in such cases varies between 40 and 60 per cent. Therefore, in every case of severe vomiting during pregnancy, one should not conclude that the patient has hyperemesis gravidarum but must consider every possible cause of vomiting. One should look especially for old laparotomy scars. The author found such scars in 22 per cent of his hyperemesis cases and he considers these suspicious of the presence of adhesions which may be the cause of a beginning ileus. Whenever doubt exists concerning a possible intestinal obstruction, an exploratory laparotomy should be performed without delay.

J. P. GREENHILL.

Dix, Victor W., and Evans, Horace: Ureteric Catheterization in Pyelitis of Pregnancy, Lancet 2: 176, 1939.

The authors reviewed a series of 84 cases of pyelitis of pregnancy which were admitted to the London Hospital during the years 1934-1937. All patients were treated with alkalinization using potassium citrate dr. 1 at two-hour intervals for eight doses and then at four-hour intervals until the patient became afebrile. Fluids are not forced but should not be less than 2,000 c.c. a day.

In 7 cases additional treatment was necessary. This consisted of ureteral catheterization with continuous drainage for four days and gave excellent results. All of this group have remained free of symptoms subsequent to delivery. In one patient a second catheterization was necessary during the course of pregnancy. Excretion pyelography and examination of the urine have shown no abnormality in 5 cases although 2 have had subsequent pregnancies. In 1 case the follow-up was incomplete. The other case seen at the sixth month of a second pregnancy was symptom free but showed pus and *B. coli* in the urine.

Where pyuria persists post partum the authors suggest the use of mandelic acid to clear up residual infection and prevent dangerous sequelae. They feel that premature induction of labor should rarely, if ever, be necessary.

CARL P. HUBER.

Bussabarger, Cuthbert, and Ivy: Studies on the Anemia of Pregnancy in Gastrectomized and Normal Dogs, J. Lab. & Clin. Med. 24: 24, 1938.

In an investigation on the anemias of pregnancy, these authors observed 5 gastrectomized dogs through a total of 15 pregnancies and a control series of 12 normal dogs through 12 pregnancies. The gastrectomized dogs were under observation from 2 to 7 years. The hematologic studies consisted of red blood counts and hemoglobin determinations, and later included hematocrit and blood volume determinations, and in 2 cases mean cell diameters. The results of this experimental series were as follows: Marked to severe anemia developed in the gastrectomized dogs in 11 pregnancies; blood volume determinations made in 8 pregnancies showed a decrease in total circulating hemoglobin of from 20 to 155 Gm. In 2 gastrectomized dogs subjected to extensive enterectomy, the anemia of pregnancy appeared to be less than before this operation. In the control dogs, marked

anemia of pregnancy occurred in 1 case; and in one, anemia of the puerperium was more marked than the anemia of pregnancy. Blood volume determinations in 8 pregnancies showed hydremia in 3 cases.

WILLIAM B. SERBIN.

Moore, Robert A., and Pastore, John B.: Note on Erythroblastic Splenomegaly Occurring During Pregnancy, Am. J. Med. Sc. 198: 187, 1939.

The reported case presents several factors which may be significant. During pregnancy the metabolism of iron is increased and the occurrence of anemia is more common than in nonpregnant women. An additional slight disturbance of the erythrocytic tissue might therefore result in conspicuous alterations. There are abundant evidences of infection in the present case: a lobar pneumonia two months before death, latent pulmonary tuberculosis, urinary infection with multiple abscess of the kidney, and a history of repeated attacks of rheumatic fever. The history of a positive Wassermann test is of doubtful significance because of the absence of anatomic changes of syphilis. It is possible that one or more of the infections, combined with pregnancy, induced the alterations of the hemopoietic tissue.

A case of conspicuous extramedullary erythropoiesis with splenomegaly but without significant alteration of the bone marrow is reported. It was associated with lobar pneumonia during pregnancy but there is insufficient evidence to determine the etiology and pathogenesis.

J. THORNWELL WITHERSPOON.

Loehnerberg, Ernst: Hemorrhage From Subserous Varix During First Stage of Labor, West. J. Surg. 47: 626, 1939.

Hemorrhages from ruptured varicose veins of the genital organs are rare but serious complications of pregnancy. Varices are commonly found in the external genitalia, and only rarely on the surface of the uterine body. Rupture of internal varicosities is not very unusual, but extremely serious because the resulting hemorrhage is sudden, severe, unanticipated, and often so rapid that medical aid comes too late.

One personally observed case of this sort is reported by the writer. Patient was first seen with a spontaneous abortion attributed to a fixed retroversion. She conceived again three years later. Ten days before expected confinement the patient experienced mild uterine contractions accompanied by occasional very severe pain in lower abdomen. Contractions stopped. Two days later patient was found to be extremely anemic. Pulse fast and thready. Abdomen greatly distended and tender. Cervix dilated to 3 cm., head movable above inlet. Diagnosis of severe internal hemorrhage was made, premature detachment of normally inserted placenta being suspected. During preparation for section patient became progressively worse, finally pulseless. Laparotomy revealed an enormous mass of free blood in abdomen. An asphyxiated child weighing 3,780 Gm. was delivered which could not be resuscitated. Inspection showed a ruptured varix on the posterior surface of the uterus, 4 cm. above cervical level. To save time uterus was amputated. Patient recovered after a stormy convalescence.

Of 13 cases found in literature, 6 were saved. In only one instance a correct preoperative diagnosis had been made.

HUGO EHRENFEST.

Brown, Clark E., and Eder, Lawrence F.: Acute Puerperal Hypophyseal Necrosis With Report of a Fatal Case, Am. J. M. Sc. 198: 166, 1939.

An acute thrombosis and necrosis of the anterior pituitary, terminating fatally during the puerperium, occurred in a woman aged 46 years. An endocrine deficiency resulted therefrom. Acute pituitary necrosis may be a more common puerperal complication than is usually recognized. Should the puerperal course of a patient progress unfavorably without obvious cause, blood sugar studies, active glucose therapy, and anterior pituitary extracts should be in order.

J. THORNWELL WITHERSPOON.

Portes and Varangot: Indications for Oophorectomy During Pregnancy, *Gynéc. et obst.* 39: 98, 1939.

It is not necessary to remove every ovarian cyst diagnosed during pregnancy. If an operation must be performed it should be carried out as late as possible. Ovarian cysts should not be removed unless they produce mechanical effects or if they are infected. Complications include torsion, hemorrhage and suppuration. If an operation is performed, the corpus luteum should not be removed. This is readily accomplished if the corpus luteum is in the healthy ovary, but even if it is in the ovary which contains the cyst, the latter may usually be shelled out leaving the yellow body in place. If it is impossible to save the corpus luteum the patient should receive massive injections of progesterone every day for a long time, instead of counting on the secretory activity of the placenta.

J. P. GREENHILL.

Brindeau, A.: Aseptic Necrobiosis of Fibromyomas in Pregnant Women, *Rev. franc. de gynéc. e d'obst.* 34: 193, 1939.

Among 59 women operated upon for aseptic necrobiosis of fibroids during pregnancy, 5 died. In 18 cases Brindeau performed a hysterectomy and in this group 2 women died. In 41 cases he performed a myomectomy and of these 3 died. In 88 per cent of the cases where myomectomy was performed the pregnancy continued uninterruptedly. It is Brindeau's belief that aseptic necrosis of fibroids is a very frequent occurrence during pregnancy, which seldom produces disturbances. When complications occur they are due to acute necrosis, a rapid hypertrophy of the fibroid, torsion of the pedicle, infection or marked change in the general condition.

Treatment consists of the following: When the necrosis is uncomplicated, conservatism should be practiced. Surgical intervention is necessary only when complications arise. Myomectomy is the treatment of choice. During labor if the tumor does not produce dystocia, delivery should be permitted to take place through the vagina. If, however, the tumor blocks the exit of the child, the pregnancy should be permitted to go to term or the onset of labor. Then a low cesarean section should be performed followed by myomectomy or hysterectomy. During the puerperium aseptic necrosis is usually innocuous. If infection sets in, immediate hysterectomy must be carried out.

J. P. GREENHILL.

Johnson, W. O.: Polypous Cervical and Vaginal Hyperplasias in Association With Pregnancy, *South. M. J.* 32: 577, 1939.

Eight cases are presented of hyperplasia of the vagina and cervical mucous membrane in association with pregnancy, which simulated carcinoma, but which disappeared after the termination of pregnancy. Possible causes of such hyperplasias are abnormal hormonal stimulation of the vaginal mucous membrane in association with pregnancy or deficiency of vitamins A and D. These conditions are not dependent on race and do not necessarily recur. Usual methods of cleanliness are sufficient to relieve symptoms during pregnancy. After delivery the lesions disappear and leave no scarring of the vagina. Radium therapy is not indicated, and termination of pregnancy is unnecessary. Post-partum infections have not occurred in this series, and the hyperplasias have all disappeared within two months after delivery.

J. P. GREENHILL.

Hansen, R.: Uterine Carcinoma and Pregnancy, *Ztschr. f. Geburtsh. und Frauenheilk.* 1: 49, 1939.

Carcinoma of the uterus which is associated with pregnancy almost exclusively involves the cervix. During the past three years Hansen has observed 5 cases of cervical cancer in a series of 3,500 pregnant women. The symptoms of cancer during gestation are those of the nonpregnant state, the most frequent being bleeding. There is no agreement as to the effect of pregnancy on cancer for some

believe that carcinoma grows more rapidly during gestation, whereas others maintain the reverse. There is, however, unity of opinion concerning the harmful effect of carcinoma on the course of pregnancy. In 30 per cent of the cases there is a spontaneous abortion. During labor there are two dangers, namely laceration with resultant hemorrhage and inability of the cervix to dilate. In the puerperium there always occurs extension of the carcinoma unless the uterus has been removed. Likewise the bacteria from the carcinomatous areas enter the uterus and frequently produce puerperal infection.

The treatment of carcinoma of the cervix during pregnancy is as follows:

1. At the end of pregnancy and during labor in the presence of a living child in an operable case, a Wertheim operation should be performed without opening the uterus and this should be followed by roentgen-ray therapy. In inoperable cases, a Porro operation should be performed on the unopened uterus and followed up by radium and roentgen-ray therapy. Spontaneous labor should never be awaited in any case of cancer of the cervix.

2. During pregnancy when the child is not viable, in operable cases, a Wertheim operation should be performed with postoperative radiation treatment. In inoperable cases, the uterus should be amputated and the patient receive postoperative radiation therapy.

J. P. GREENHILL.

Newell, Q. U., and Scrivener, W. C.: Pregnancy and Cervix Cancer, South. M. J. 32: 818, 1939.

The occurrence of cancer of the cervix with pregnancy is very infrequent, probably because the age group for malignancy and for childbearing do not coincide. In 27,952 obstetric admissions there were only 7 cases of carcinoma of the cervix, an incidence of 1 in 4,000. Summaries of 8 cases are presented.

Diagnosis is frequently delayed, either because vaginal bleeding is ignored by the patient, or the physician interprets the symptom as a sign of threatened abortion and neglects to make an examination. Association of cervical cancer and pregnancy is more frequent in multiparas, suggesting that the trauma of parturition may be an etiologic factor. Pregnancy probably accelerates the growth of malignancy. Bleeding during gestation should be investigated and cervical biopsy performed when indicated.

Treatment has not been standardized. Treatment of the malignancy should take precedence over consideration for the pregnancy. The authors employ the League of Nations clinical classification of pelvic cancer, and they apply therapy according to four arbitrarily designated periods of pregnancy. Up to four and one-half months, total hysterectomy followed by x-ray therapy is advocated for Groups 1 and 2. For Groups 3 and 4, cervical application of radium should precede supravaginal hysterectomy and radiation.

For a gestation of four and one-half to seven months in lesions in Groups 1 and 2 the radical operation and irradiation is preferable. As an alternate procedure, 4,000 mg. hours of radium applied to the cervix with screening to protect the fetus. Advanced lesions should be treated by high supravaginal hysterectomy and tandem insertion of radium in addition to x-ray therapy. Beyond seven months, screened radium implantation in the cervix with Porro cesarean section at term and subsequent irradiation. At or near term, the same procedure is advocated, except that radiation is prescribed after operation.

Radiation is followed by a satisfactory response, and it is relatively safe for the patient and the baby.

Vaginal delivery in these patients is contraindicated.

ARNOLD GOLDBERGER.

Theobald, G. W.: Relation of Pregnancy to Hypertension and Chronic Nephritis, J. Obst. & Gynaec. Brit. Emp. 43: 1037, 1936.

Women who normally suffer from albuminuria tend to pass protein-free urine during the first six months of pregnancy. The blood pressure normally falls during

the first half of pregnancy, and the blood pressure of women suffering from hypertension may fall within normal limits during this period of gestation. The water balance is disturbed during the second half of a normal pregnancy. This disturbance precedes hypertension, which itself precedes albuminuria. This sequence of events may be caused by hepatic malfunction and may be the result of abnormal proteins circulating in the blood. It is suggested that a high blood urea content may be considered an index of hepatic malfunction.

There are two main groups of women in whom it is possible to predicate before marriage that they are likely to suffer from pre-eclampsia or eclampsia: (1) those with glomerulonephritis resulting from the exanthems and tonsillitis; (2) those with a blood urea content exceeding 40 mg. per cent and who are unable to concentrate this substance in the urine. These women will, apart from suitable treatment, manifest toxemic symptoms in each successive pregnancy.

It is suggested that the hepatic malfunction resulting in the presence of abnormal proteins in the blood plasma is caused by a meat diet associated with a disturbance of the calcium metabolism and an insufficient intake of the vitamin B complex.

The remarkable association of heredity with the hypertension of pregnancy not only makes it reasonable to place this condition in the same category as hypertension occurring in the nonpregnant state but warrants the assumption that hypertension of pregnancy is merely an exacerbation of the insidious process which ultimately results in death.

There is no evidence of a causal relation between pregnancy and chronic nephritis. A woman with chronic glomerulonephritis may pass through pregnancy without further damaging her kidneys providing the condition has not progressed sufficiently far to embarrass her general health and certain tests for renal efficiency prove satisfactory.

Death of the fetus in utero is to be attributed to dietetic deficiencies. If it is true that hypertension of pregnancy presents an exaggerated picture of the march of hypertension in man, then it is obvious that the obstetrician has the unique opportunity of contributing to knowledge of the early stages of chronic glomerulonephritis and of the causation of some forms of arteriosclerosis and renal failure, for he sees the patient ten years before she consults the physician with symptoms attributable to the conditions. If there is no causal relation between pregnancy and chronic nephritis the last need for postulating a pregnancy toxin has disappeared.

J. P. GREENHILL.

Page, E. W., and Cox, A. J.: Renal Changes Following Toxemias of Late Pregnancy, West. J. Surg. 46: 463, 1938.

Clinical follow-up studies on 96 cases of eclampsia substantiate the findings in the collected literature that recurring toxemias, hypertension and albuminuria are frequent sequelae of the toxemias of later pregnancy. The nature of the residual renal lesion following eclamptogenic toxemias was investigated by the examination of kidney tissue from 26 selected autopsies. Thickened glomerular capillary membranes were demonstrated in the kidneys of eight patients dying during toxemias of late pregnancy. Seven women who were known to have had previous toxemias of varying severity, and who died of miscellaneous causes, uniformly showed similar changes in the glomerular capillary membrane. This glomerular lesion is not specific for eclampsia since slight degrees of similar changes were found in five of 11 women who had had normal pregnancies and who died from various causes unrelated to eclampsia.

J. P. GREENHILL.

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